

**REVIEW ON: SYNTHESIS AND BIOLOGICAL EVALUATION OF  
DIFFERENT BENZOTHAIAZOLE DERIVATIVES**

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**ABSTRACT**

Benzothiazole is aromatic compound most effective ion heterocyclic classes with molecular formula  $C_7H_5NS$ . It is colorless, gradual viscous liquid. The reported activities are most effective substituted derivatives. These derivatives are synthesis of benzothiazole moiety which comprises with different biological activities. In this review the different benzothiazole derivatives compound as synthesis of 2-[2-(N,N-dichloroethylamino)-4-fluorophenyl]-benzothiazole or synthesis of 2-amino acetate, 6-chloro benzothiazole are made to synthesize by large number of efforts and their other derivatives were found to possess antimicrobial, anti-inflammatory, anticonvulsant, anti-helminthic, antidiabetic, antitumor, cyclooxygenase inhibitor, anti-alzheimers and antimalarial activities. Benzothiazole moiety is very

small but it possesses different biological activities but not only benzothiazoles but its different substituted derivatives also give different biological activities. Benzothiazoles are remarkably effective compounds after extensive structural modification. These are most effective against different strains of microorganisms. This review is focused on the benzothiazole moiety and its different derivatives that possess different biological activities. Among these heterocyclic 1,3-benzothiazole derivatives that attracted considerable attention in the research sector of synthesis, because of its potent and significant pharmacological

activities.

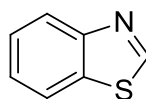
**KEYWORDS:** Benzothiazole derivatives, Anti-inflammatory, Anti-microbial and Anti-helminthic.

## INTRODUCTION

Benzothiazole is aromatic compound most effective ion heterocyclic classes with molecular formula  $C_7H_5NS$ . It is colorless, gradual viscous liquid. Thiazole is structurally related to thiophene and pyridine. Thiazole (a) was first described by **Hantzschant Waber** in 1887. **Popp** confirmed its structure in 1889. The ultimate structure of benzothiazole (b) consists of benzene ring fused with 4 or 5 position of thiazole. A brief account of some commonly used methods to synthesize as well as cyclization of benzothiazole derivatives by using different types of catalysts and various structural alterations conducted on benzothiazole ring and preferential specificities imparted in their biological responses.<sup>[1]</sup> The parent compound, benzothiazole is not far and wide used, many of its derivatives are found adaptable in industrial products or in natural history.



(a)



(b)

### Chemical Structure of Thiazole (a) and Benzothiazole (b).

Sugars and their derivatives, for instance, exist in the form of five-members or six-member rings contain oxygen atom. Most member of vitamin B group obtained heterocyclic ring containing nitrogen. One example is vitamin B6 which is a derivative of pyridine, essential in amino acid metabolism. Heterocyclic compounds are very widely distributed in nature and are essentials to life in various ways.<sup>[2]</sup>

Benzothiazole is a heterocyclic aromatic organic compound. It is an important pharmacophore and a privileged structure in a medicinal chemistry. This compound is bicyclic in nature which consists of the fusion of benzene and thiazole. Now a day, a moiety of choice which possesses many pharmacological properties. The most important compound in nature vitamin B group possess heterocyclic ring containing nitrogen and example is vitamin B6. Benzothiazoles are fused member rings, which contain the heterocyclic bearing thiazole, sulphur and nitrogen atoms constitute.<sup>[3]</sup>

Benzothiazole is a bicyclic ring system. It contains a benzene ring fused to a thiazole ring. The simple benzothiazole nucleus is present in compounds involved in research aimed at evaluating new products that possess interesting biological activities like antimicrobial, anti-tubercular, antitumor, antimalarial, cyclooxygenase inhibitor, antidiabetic, anticonvulsant, analgesic or anthelmintic. Benzothiazoles play a vital role in the field of medicinal chemistry. Benzothiazole moiety is an important part of a molecular structure that is responsible for a particular biological or pharmacological interaction that it undergoes.

Benzothiazoles are bicyclic ring system with multiple applications. In 1950, a number of 2-aminobenzothiazoles were intensively studied as central muscle relaxants. Since then chemists have not taken active interest in this chemical family. Biologist's attention was drawn to this series when the pharmacological profile of Riluzole was discovered. Riluzole (6-trifluoromethoxy-2-benzothiazolamine) was found to interfere with glutamate neurotransmission in biochemical, electrophysiological biphasic and behavioural experiments. After that benzothiazole derivatives have been studied extensively and found to have diverse chemical reactivity and broad spectrum of biological activity.<sup>[4]</sup>

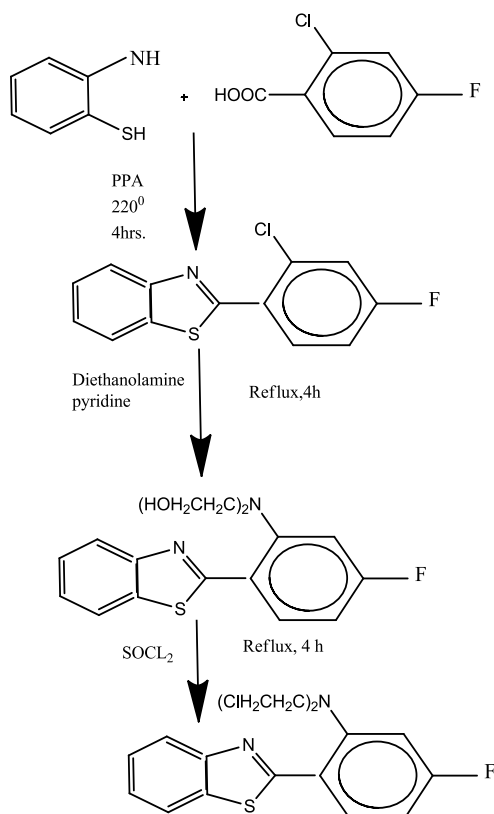
Benzothiazoles show antitumor activity, especially the phenyl-substituted benzothiazoles, while condensed pyrimidobenzothiazoles and benzothiazoloquinazolines exert antiviral activity. Recently, described the synthesis of bis-substituted amino benzothiazoles as potential anti HIV agents. Substituted 6-nitro-and 6-aminobenzothiazoles show antimicrobial activity. Sugar and their derivatives together with vitamin C for instance, exist in the form of five-membered (furan) or six membered (pyran) rings containing one oxygen atom. Most member of vitamin B group contained heterocyclic ring containing nitrogen, example is vitamin B<sub>6</sub> (pyridoxine), which is a derivative of pyridine, essential in amino acid metabolism. Benzothiazole is a weak base heterocyclic compound having varied biological activities and still of great scientific interest now a days. Other than this widely found active in bio-organic and medicinal chemistry, that utilized in drug discovery.<sup>[5]</sup>

## SYNTHESIS OF BENZOTHAZOLE DERIVATIVES

### 1. Synthesis of 2-[2-(N,N-dichloroethylamino)-4-fluorophenyl]-benzothiazole:-

Equimolar quantities of o-aminothiophenol (0.04 mol) and 2-amino-4-fluorobenzoic acid were added to 15 g of polyphosphoric acid (PPA) and refluxed for 4 hrs. at 220°C. The reaction mixture was cooled and poured in ice cold about 10% sodium carbonate solution.

The precipitate was filter and recrystallized from methanol to find 2-(2-amino-4-fluorophenyl)-benzothiazole. 2-(2-amino-4-fluorophenyl)-benzothiazole (0.01 mol) and 0.01 mol of diethanolamine were dissolved in 25 ml of pyridine and refluxed for 4 hrs. Cooled and poured in cold water. The mixture was filtered after 1 hr and the precipitate recrystallized from methanol to get 2-[2-(N,N-dihydroxyethylamino)-4-fluorophenyl]-benzothiazole. 2-[2-(N,N-dihydroxyethylamino)-4-fluorophenyl]-benzothiazole (0.01) was refluxed with 0.03 mol of thionyl chloride for 4 hrs. The undesirable of thionyl chloride was removed by distilling with benzene. After distillation, the residue was collected, washed with cold water and recrystallized from ethanol. 2-[2-(N,N-dichloroethylamino)-4-fluorophenyl]-benzothiazole is prepared.<sup>[6]</sup>

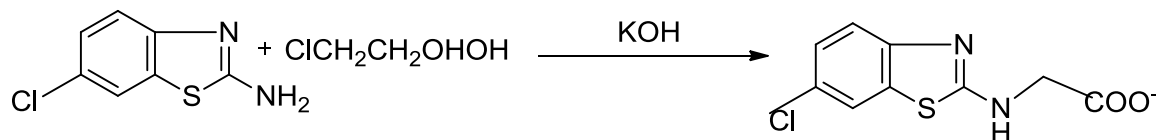


### 2-[2-(N,N-dichloroethylamino)-4-fluorophenyl]-benzothiazole.

#### 2. Synthesis of 2-amino acetate, 6-chloro benzothiazole:-

A solution of 95% acetic acid (50 ml) or p-chloro aniline (0.085 mol) was added to a solution of KSCN (0.308 mol) in 95% acetic acid (100 ml). The mixture was cooled & a solution of Br<sub>2</sub> (7.5 ml) in acetic acid (30 ml) was added slowly with stirring so that temperature between 10 to 100°C. After adding was complete, the stirring was continued for 1hr. at 50°C and then mixture was poured into water. The solid was collected & re-crystallized from ethanol. The

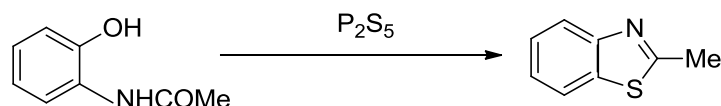
product (0.036 mol), conc. HCl (27 ml) and water (50 ml) were refluxed for 2 hrs. The solution was cooled and the product was filtered off, washed with water & re-crystallized from ethanol.<sup>[7]</sup>



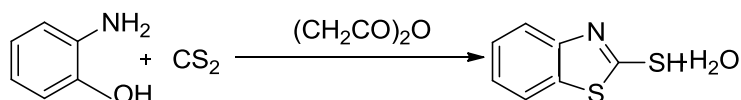
**2-amino acetate, 6-chloro benzothiazole.**

## REACTIONS OF BENZOTHAZOLE DERIVATIVES

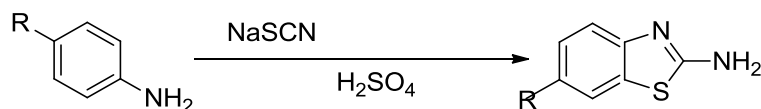
Benzothiazole are also formed by act of phosphorus pentasulfide on O-acylaminophenols.<sup>[5]</sup>



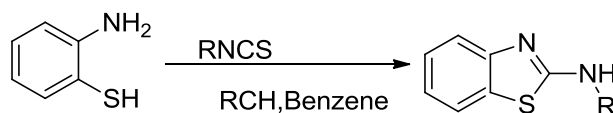
2-mercaptobenzothiazole is vulkanisation accelerator be prepared as follows.<sup>[5]</sup>



Sodium thiocyanate and cyclize p-substituted aniline were used into 2-amino-6-Substituted benzothiazole in the presence of sulfuric acid which act as a catalyst.<sup>[8]</sup>



Synthesis the cyclizations of isothiocyanates to 2-aminobenzothiazole in presence of benzene which act as a catalyst.<sup>[8]</sup>

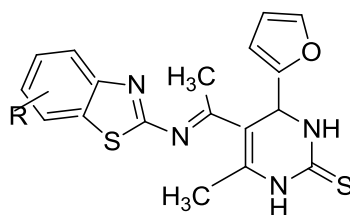


## PHARMACOLOGICAL STUDY OF BENZOTHAZOLE DERIVATIVES

### Antimicrobial Activity:-

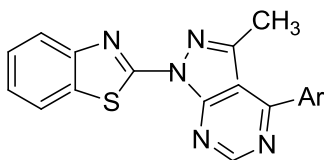
1. Substituted derivatives of 5-[(1E)-N-(1,3-benzothiazol-2-yl)ethanimidoyl]-4-(furan-2-yl)-3,4-dihydropyrimidine-2(1H)-thiones were prepared from commercially available 2-amino benzothiazole. Compounds were also synthesized by microwave irradiation method. Yields of microwave assisted synthesis were high. Synthesized compounds were tested for Gram positive and Gram negative bacterial cultures. All the compounds were found to exhibit good

to moderate antibacterial activity. Erythromycin used as standard drug.<sup>[9]</sup>



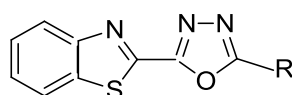
Where R=H, -Cl, CH<sub>3</sub>, -Cl, -NO<sub>2</sub>, -OC<sub>2</sub>H<sub>5</sub>

2. Standard strains were procured from the National Collection of Industrial Microorganism, National Chemical Laboratory, India. Synthesized 1-(1,3-benzothiazol-2-yl)-3-methyl-4-substituted phenyl-1H-pyrazolo[3,4-d]pyrimiding derivative compounds were tested [50 and 100 µg ml<sup>-1</sup> in sterile dimethyl sulfoxide (DMSO)] for their in vitro antimicrobial activity by the cup plate diffusion method. The antibacterial activity was evaluated on nutrient agar plates at 37 °C for 24 hours against Gram-positive bacteria *Staphylococcus aureus*, *Bacillus megaterium*, Gram-negative bacteria *Escherichia coli* and *Pseudomonas aeruginosa*. Ciprofloxacin used as control drugs as 10 and 20 µg/ml solutions, respectively, in sterile dimethyl sulfoxide. Average diameter of inhibition zone (three independent evaluations) of bacterial growth around the disk in mm.<sup>[10]</sup>

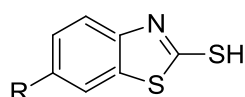


Where Ar = C<sub>6</sub>H<sub>5</sub>, Cl-C<sub>6</sub>H<sub>4</sub>, OH-C<sub>6</sub>H<sub>4</sub>, OCH<sub>3</sub>-C<sub>6</sub>H<sub>4</sub>, di-OCH<sub>3</sub>-C<sub>6</sub>H<sub>3</sub>, NO<sub>2</sub>-C<sub>6</sub>H<sub>4</sub>, N(CH<sub>3</sub>)<sub>2</sub>-C<sub>6</sub>H<sub>4</sub>, CH=CH-C<sub>6</sub>H<sub>5</sub>, 2-fury.

3. 2-(5-substituted-1,3,4-oxadiazole-2-yl)-1,3-benzothiazole synthesis compounds In vitro antibacterial activity against gram positive and gram negative bacterial strains such as *Bacillus subtilis*, *Bacillus pumilus*, *Escherichia coli* and *Pseudomonas aureginosa* at concentration 100 µg/ml by disc diffusion method by using DMSO as solvent control and nutrient agar was employed as culture media. After 24 hr of incubation at 37<sup>0</sup>C, the zone of inhibition was measured in mm. The activity was compared with standard drug antibiotic Ciprofloxacin.<sup>[11]</sup>

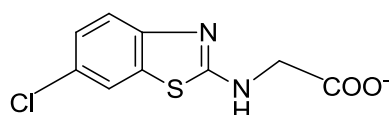


4. Antimicrobial activity was estimated by using National Committee for Clinical Laboratory Standards (NCCLS, 2003) assay Antimicrobial studies of 2-mercepto 1,3-benzothiazole derivatives. It was observed that the synthesized compounds substituted with a S-H moiety at the 2-position of the heterocyclic nucleus favored the anti bacterial activity especially against the Gram-positive strains. Among the series the most prominent and consistent antimicrobial activity was obtained with compound (MIC: 3.2  $\mu\text{g/ml}$ ) carrying a trifluoromethyl moiety at the 6-position of the heterocycle. Compound show an appreciable broad spectrum of action against both Gram-positive and Gram-negative bacteria. Its MIC value (25 $\mu\text{g/ml}$ ) toward *E.coli* is very significant. Norfloxacin antibiotic used as standard drug.<sup>[12]</sup>

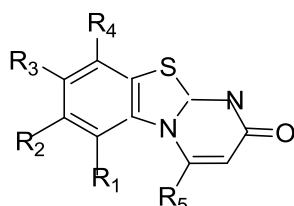


Where R = CH (CH<sub>3</sub>)<sub>2</sub> Cl, CH<sub>3</sub>, OCH<sub>3</sub>, CF<sub>3</sub>, F, H, NH<sub>2</sub>, OCH<sub>2</sub>CH<sub>3</sub>, NO<sub>2</sub>.

5. 2-Amino acetate, 6-chloro benzothiazole was screened for their antimicrobial activity using disc diffusion method. The bacterial organisms used included both gram positive and gram negative strains like *Staphylococcus aureus*, *Escherichia coli*, *Streptococcus pyogens*, *Salmonella typhi*, *S.entricasertyphi* and *Micrococcus luteus*. The sterile disc of 6mm diameter was loaded with 20 $\mu\text{l}$  of title compound solution (1000 $\mu\text{g/ml}$ ) in DMF.<sup>[7]</sup>



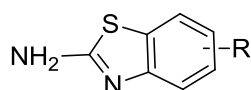
6. Various approaches were made to check the role of benzothiazole moiety as antimicrobial agent from the discovery of molecule to the present scenario. Synthesis of series of pyrimido [2,1-b] benzothiazoles by conjugation addition to nitrogen of 2-aminobenzothiazoles to alkyne  $\hat{\alpha}$ -carbon atom of acetylenic acid followed by ring closure and synthesized compounds are studied for antimicrobial activity against *E. coli* and *Enterobacter* as test organisms at conc. 100 $\mu\text{g}$  per disc using Vancomycine and Meropenam as standard drug.<sup>[13]</sup>



$R_1=H$ ,  $R_2=Cl$ ,  $R_3=H$ ,  $R_4=H$ ,  $R_5=Ph$

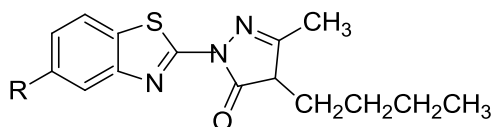
### Anti-inflammatory Activity:-

1. Benzothiazole based anti-inflammatory agents have been synthesized. Some novel 2-amino benzothiazole derivatives and evaluated them for anti-inflammatory activity. Test compounds showed significant for anti-inflammatory activity and it was noted that when the 2-amino benzothiazole is substituted at 4 or 5 positions with electron withdrawing group like Cl, NO<sub>2</sub>, OCH<sub>3</sub>, increase in anti-inflammatory activity was found.<sup>[14]</sup>



$R=H$ , Cl

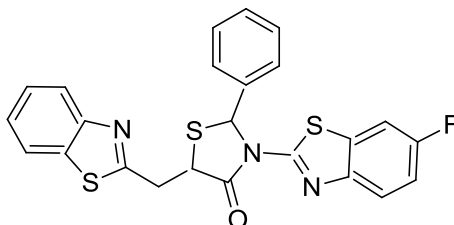
2. Prepared some new 2-(4'-butyl-3', 5'-dimethylpyrazol-1'-yl)-6-substituted benzothiazoles and 4-butyl-1-(6'-substituted-2'-benzothiazolyl)-3-methylpyrazol-5-ones and were found to display significant anti-inflammatory activity.<sup>[15]</sup>



$R=H$ , Cl, F, CH<sub>3</sub>, OCH<sub>3</sub>

### Antidiabetic Activity:-

Synthesized 2-amino[5'-(4-sulphonylbenzylidene)-2,4-thiazolidinedione]-7-chloro-6-fluorobenzothiazole series and screened for their antidiabetic activity on albino rat by alloxan induced tail tipping method.<sup>[16]</sup>

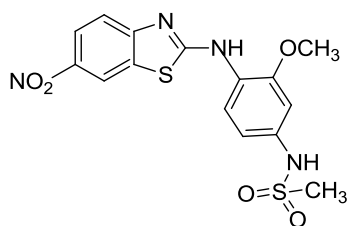


### Antimalarial Activity:-

Antimalarial activity of 2-substituted-6-nitro and 6-amino benzothiazoles and their anthranilic acids were carried out on W2 and 3D7 strains of *P. falciparum*. The results revealed the potency of compounds as the antimalarial agents of clinical and biological

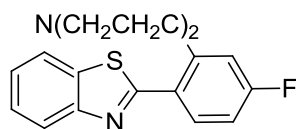


research.<sup>[17]</sup>

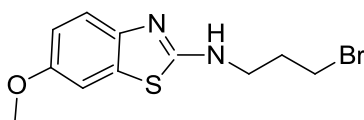


### Anticancer Activity:-

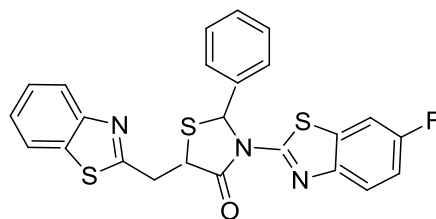
1. Refluxed o-aminophenols with substituted benzoic acid in presence of polyphosphoric acid at higher temperature to get aryl substituted benzothiazoles and evaluated them against Human Cervical Cancer cell lines.<sup>[6]</sup>



2. A huge number of benzothiazoles derivatives have show strong anticancer activity. Some of the recent fiction reports are summarized in this segment. Novel derivatives of N-alkylbromo-benzothiazoles have been evaluated for their anticancer potency. The majority of the compounds in this series have shown significant cytotoxic activity. However, complex (3-bromo-propyl)-(6-methoxy-benzothiazol-2-yl) amine has been found to be the most promising anticancer agent.<sup>[18]</sup>

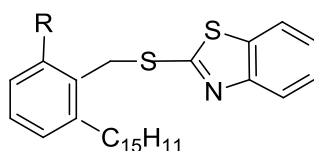


3. Synthesized some of the novel bis-benzothiazole derivatives, compounds synthesized were screened for in-vitro anticancer activity against (Human Epithelial cervix cancer cell line) HeLa cell lines by MTT [3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyl tetrasolium bromide] assay method along with control. All the newly synthesized compounds were screened for anticancer activity at a concentration of 100, 10, 1, and 0.1  $\mu$ M. All compounds showed good anticancer activity against Human Epithelial cervix cancer cell lines.<sup>[19]</sup>



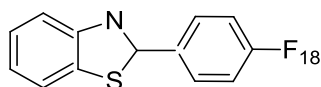
### Cyclooxygenase inhibitor Activity:-

Pyrazolones and pyrazolinones rank among the more revered non steroidal anti-inflammatory agents. Phenylbutazone and its congeners incorporating a pyrazoline structure are more potent anti-inflammatory agents. In the recent years a number of Benzothiazole derivatives have been synthesized and found to display anti-inflammatory activity. Synthesis a series of 2-[(2-alkoxy-6-pentadecylphenyl) methyl] thio-1-H-benzimidazoles/benzothiazole from anacardic acid (pentadecylsalicylic acid) and investigated their ability to inhibit human cyclooxygenase enzyme -2 standard drug.<sup>[20]</sup>



### Antialzheimers Activity:-

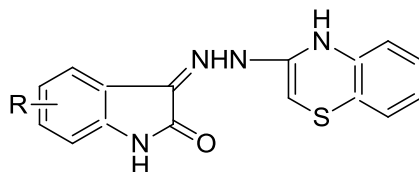
2-Floro phenyl benzothiazoles evaluated, it as amyloid imaging agent in Alzheimers disease in comparison with [11C]PIB (11C labeled 6-hydroxy-2-(4''-N- [11C] methylaminophenol)-1,3- benzothiazole and showed excellent characteristics comparable with those of [11C]PIB, namely superior affinity for amyloid plaques present in human Alzheimers disease.<sup>[21]</sup>



### Anthelmintic Activity:-

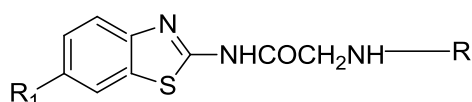
1. The synthesized compounds [3-(2-Hydrazino benzothiazoles)-substituted indole-2-one] were screened for anthelmintic activity by using earthworms. Indian adult earth worms (*Pheretima Posthuma*) of nearly equal size about 6 cm in length and 0.2-0.3 in width were placed in standard drug solution and test compound solution at room temperature. Normal saline was used as a control. The standard drug and test compounds were dissolved in minimum quantity of DMF (dimethyl formamide) and make up the volume equal to 15 ml with normal saline (NS) to get the concentration of 0.1% w/v, 0.2% w/v and 0.5% w/v. Albendazole was used as standard drug, complete paralysis and death of earth worms. The

mean lethal time for each test compound was recorded and compared with standard drug.<sup>[22]</sup>



Where R = -H, -5-COOH, 5-CH<sub>3</sub>, 5-Cl, 5-NO<sub>2</sub>, -5-Br.

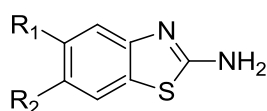
2. The newly synthesized compound N-(benzo[d]thiazol-2-yl)-2-chloroacetamide were tested for anthelmintic activity. *Pheretima posthuma* (Indian adult earthworms) of nearly equal size were selected at random for present study. The earthworms were divided into four group of six earth worms in each. Albendazole diluted with normal saline solution to obtain 25 mg/ml and 50 mg/ml served as standard and poured into petridishes. The synthesis compounds were prepared in minimal quantity of DMSO and diluted to prepare two concentration 25 mg/ml and 50 mg/ml for each compound. Normal saline served as negative control. Six earthworms nearly equal size are taken for each concentration and placed in petridishes at room temperature. The mean time for paralysis was noted when no movement of any sort could be observed, except when the worm was shaken vigorously; the time death of worm was recorded after as certaining that worms neither moved when shaken nor when given external stimuli. In the same manner albendazole was included as reference compound.<sup>[23]</sup>



Where R<sub>1</sub> = Br, NO<sub>2</sub>

R = Various amines

3. The synthesized compounds (2-amino-5, 6-substituted benzothiazole) were evaluated against two different earth warm species *Eudrilus eugeniae* and *Megascoplex konkanensis* at 200 mg/10 ml concentration following Garg's method. Tween 80 (15%) solution in distilled water was used as a control and Mebendazole was used as a control. The paralysis and death times were noted and their mean was calculated for triplicate sets.<sup>[24]</sup>

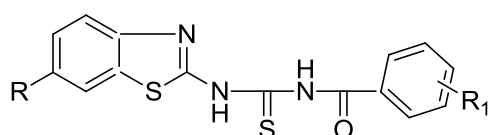


Where R<sub>1</sub> = Cl, F, Br, NO<sub>2</sub>, CH<sub>3</sub>, C<sub>2</sub>H<sub>5</sub>, OCH<sub>3</sub>, CH<sub>3</sub>

$R_2 = \text{H, CH}_3$

### Anticonvulsant Activity:-

The synthesized N-{[(6-Substituted-1,3-benzothiazole-2-yl)amino] carbonothioyl}-2/4-substituted benzamides. The anticonvulsant evaluations were undertaken by the National Institute of Health, using their reported procedures. Male albino mice (CF-1 strain, 25-30g) and male rats (Sprague-dawley, 100-150g) were used as experimental animals. The test compounds and standard drug were administered intraperitoneally suspended in Tween 80 (1%) or in 0.5% methyl cellulose-water mixture.<sup>[25]</sup>

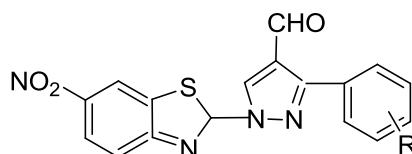


$R = \text{Br, Cl, F, NO}_2, \text{CH}_3, \text{OCH}_3$

$R_1 = \text{H, Cl, OCH}_3$

### Antitubercular Activity:-

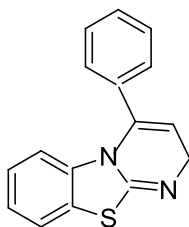
1. 6-Nitro-2-[4-formyl-3-(substituted phenyl) pyrazol-1-yl] benzothiazoles were synthesized and screened for antitubercular activity against H<sub>37</sub>RV strain of Mycobacterium tuberculosis by proportion method on Lowenstein Jensen. 6-Nitro-2-[4-formyl-3-(substituted phenyl) pyrazol-1-yl] benzothiazoles exhibit a range of activities in the antitubercular screens. Compounds emerged as the most promising active compounds comparable to that of standards.<sup>[26]</sup>



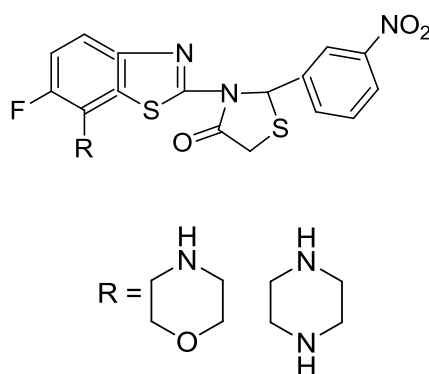
$R = \text{H, OH, Br, NO}_2, \text{OCH}_3, \text{OH, Cl, F, CH}_3, \text{diOCH}_3$

2. 4-Phenyl-2H-pyrimido[2,1-b][1,3]benzothiazole derivatives were synthesized by the condensation of 2 amino benzothiazole derivatives, as beta keto ester, and aromatic aldehyde and the synthesized compounds were characterized by IR, <sup>1</sup>H NMR and GC MASS spectroscopy. These compounds investigated for anti-tubercular activities by MABA (Microplate Alamar Blue Assay) method. The most promising anti Tuberculosis activity compound showed minimum inhibition concentration at 6.25 g/ml that is equivalent to the

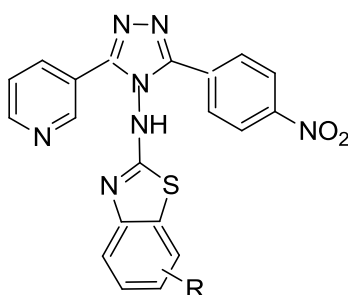
standard drugs like Pyrazinamide, Ciprofloxacin and Streptomycin. The synthesized molecules were screened for their activity to inhibit the growth of the Mycobacterium Tuberculosis. Two hundred micro litter of deionised sterile water added to all outer perimeter wells of sterile wells plate. This is to reduce evaporation of medium in the test wells during incubation. 100µl of middle brook 7H9 broth and run solvent of compounds added directly on 96 wells plates. The final drug concentrations tested ranges as of 100 to 0.2 micro gram/ml. Plates were enclosed. Incubated at 37<sup>0</sup>C for 5-6 days. After this, 1:1 mixture of freshly prepared Alamar blue reagent and 10% tween 80 (25µl) of was added in the plate and incubated for 24 hrs. A blue colour in the well was interpreted as negative bacterial growth, and pink colour was scored as increase. The minimum inhibitory concentration (MIC) is defined as lowest drug concentration, which prevents the colour change from blue to pink.<sup>[27]</sup>



3. 4-Fluoro-3-chloroaniline treated with potassium thiocyanate in presence of Glacial acetic acid (GAA) and bromine was converted into 2-amino-6-fluoro-7-chlorobenzothiazole. The synthesized compound in presence of m-nitro benzaldehyde refluxed in ethanol to obtained 3-[6'-fluoro-7'-chloro(1',3') benzo thiazol-2'-yl]-m-nitrophenyl(1,3) thiazolidine-4-one. The above said compound was treated with ortho, Meta and P-nitro anilines, ortho, meta, p-chloro anilines, morpholino, Piperazine, diphenylamine with DMF to obtain different derivatives. Some compounds shows potential anti mycobacterial activity. Sterile Kirchner's medium was dispensed in test tube and to this sterile horse serum (0.5 mL) was added. The stock solution was sterile by passing through a 0.2 mm polycarbonate sterile membrane filters. Further the serial dilution of test compounds were carried out. Test compounds at different concentrations were added to culture medium in a sterilized test tube and strain of Mycobacterium Tuberculosis was inoculated at about 10<sup>6</sup> bacilli/ml concentration. The tubes were incubated at 37<sup>0</sup>C for 21 days and examined the presence or absence of growth of the investigation organisms. The lowest concentration, which showed no visible growth, was taken as the end point i.e. minimum inhibitory concentration (MIC). Standard drugs were used as Rifampin and Isoniazide for anti mycobacterium activity.<sup>[28]</sup>



4. Here the synthesis and in vitro antimicrobial and ant tubercular activity of a variety of series of 3-(3-pyridyl)-5-(4-nitrophenyl)-4-(N-substituted-1,3-benzothiazol-2-amino)-4H-1,2,4-triazole. Anti-tubercular activity, using agar method. Drug susceptibility and determination of minimum inhibition concentration of the test compounds against Mycobacterium Tuberculosis were performed by agar, minimum inhibition concentration method 24–29 where primary 1000, 500, 250 and secondary 200, 100, 62.5, 50, 25, 12.5, 6.25, 3.25  $\mu\text{g/ml}$  dilutions of each test compound were added, liquid medium and then media were sterilized by inspissation method. A culture of Mycobacterium Tuberculosis increasing on medium was harvested in 0.85% saline in bijou bottles. All test compounds that make first stock solution of 2000  $\mu\text{g/ml}$  concentration of compounds were prepared in DMSO. These tubes were then incubated at 37°C for 24 h followed by streaking of Mycobacterium Tuberculosis. These tubes were then incubated at 37°C. For 12 days. Growth of bacilli was show after 12 days, 22 days, and finally 28 days of incubation. Tubes having the compounds were compared with control tubes where medium alone was incubated with Mycobacterium Tuberculosis. The concentration at which no development of colonies occurred or <20 colonies was taken as MIC of test compound. The standard strain Mycobacterium Tuberculosis was tested with known drug Rifampicin.<sup>[29]</sup>



R = F, CH<sub>3</sub>, Cl, Br, OCH<sub>3</sub>, NO<sub>2</sub>

## CONCLUSION

The benzothiazoles and their derivatives have shown a wide range of biological activities. It is a adaptable nucleus in the field of Pharmaceutical chemistry. Thus this matchless molecule must serve as future therapeutic leads of developing a variety of biological agents. The biological profiles of this new generation of benzothiazoles signify much progress with regard to the elder compounds. Benzothiazole is an important class of heterocyclic compounds and exhibits a variety of pharmacological activities. In this review, we have emphasized on the biological assortment of benzothiazoles, their synthetic methodology and recent developments in this field during the most recent few years. Variety of benzothiazoles have been developed in last few years possessing considerable antitubercular, antimicrobial, antimalarial, anticonvulsant, anthelmintic, analgesic, anti-inflammatory, antidiabetic and anticancer activities etc.

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