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## A COMPREHENSIVE REVIEW ON BENZOTHAIAZOLE DERIVATIVES FOR THEIR BIOLOGICAL ACTIVITIES

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### Keywords:

Benzothiazoles, Anticancer, Antimicrobial, Antioxidant

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**ABSTRACT:** Benzothiazole derivatives have a wide interest because of their diverse biological activities and clinical use. This bicyclic compound consists of a fusion of benzene nucleus with a five-membered ring comprising nitrogen and sulphur atoms. It is a vital Pharmacophore and privileged structure in medicinal chemistry and exhibits various useful therapeutic activities such as anti-tubercular, antimicrobial, antimalarial, anticonvulsant, anthelmintic, anti-inflammatory, anti-tumor, anti-diabetic, analgesic, neurodegenerative disorders, local brain ischemia, and central muscle relaxant activities. Moreover, it can be easily found in a range of marine or terrestrial natural compounds that have tremendous biological activities. Benzothiazoles have a promising biological profile and are easy to access which makes this pharmacophore an interesting molecule for designing new bioactive benzothiazole derivatives.

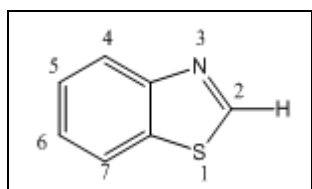
**INTRODUCTION:** Heterocyclic compounds containing oxygen, nitrogen and sulphur atoms have been identified to have the most significant biological activities<sup>1</sup>. Benzothiazole is a heterocyclic aromatic compound. The compound is bicyclic which consists of a fusion of benzene with thiazole ring. It is an important pharmacophore as benzothiazole and its novel analogs have been found to have a wide variety of therapeutic activities in medicinal chemistry<sup>2</sup> such as in anticancer<sup>3-6</sup>, anti-HIV<sup>6</sup>, antioxidant<sup>7</sup>, anticonvulsant<sup>8</sup>, trypanocidal agent<sup>9</sup>, antitumor<sup>10-13</sup>, antimicrobial<sup>14</sup>, COX inhibitor<sup>15</sup>, hypoglycemic<sup>16</sup>, antidiabetic<sup>17</sup>, antituberculosis<sup>18</sup>, anti-urease<sup>19</sup> and inhibitor of  $\alpha$ -glucosidase<sup>20</sup>.

Benzothiazole is a six-membered bicyclic heteroaromatic compound in which benzene ring is fused to the 4- and 5-positions of thiazole ring. Benzothiazoles are found in marine as well as terrestrial natural compounds in a very less amount but have considerable pharmacological effects, where they act as aroma constituents of tea leaves and cranberries which are produced by fungi named *Aspergillus clavatus* and *Polyporus frondosus*. The fission yeast *Schizosaccharomyces pombe* is an important organism for the study of cellular biology.

As eukaryotes, these yeasts can be used to study processes that are conserved from yeast to humans but are absent from bacteria, such as organelle biogenesis or to study the mechanism such as transcription, translation and DNA replication, in which the eukaryotic components and processes are significantly different from their bacterial counterparts<sup>21</sup>. The data can be calculated by DFT methods; its importance is given in various recent publications<sup>22</sup>.

<p><b>QUICK RESPONSE CODE</b></p> 	<p style="text-align: center;"><b>DOI:</b> 10.13040/IJPSR.0975-8232.10(7).3196-09</p> <hr/> <p style="text-align: center;">The article can be accessed online on <a href="http://www.ijpsr.com">www.ijpsr.com</a></p>
<p><b>DOI link:</b> <a href="http://dx.doi.org/10.13040/IJPSR.0975-8232.10(7).3196-09">http://dx.doi.org/10.13040/IJPSR.0975-8232.10(7).3196-09</a></p>	

Various benzothiazole derivative such as 2-aryl benzothiazole is in the eyes of most scientists due to its diverse structure and its uses as radioactive amyloid imaging agents. It is reported that the isosters and derivatives of benzothiazole have antimicrobial activity against various types of gram positive and gram negative bacterias (e.g., *E. coli*, *Pseudomonas aeruginosa*, *Enterobacter Staphylococcus epidermis*, etc.). The various positions in the benzothiazole ring are indicated accordingly sulphur having 1 position as shown in the figure.



1, 3- Benzothiazole

**Molecular Formula:** C<sub>7</sub>H<sub>5</sub>NS

**Molecular Weight:** 135.184 g/mol

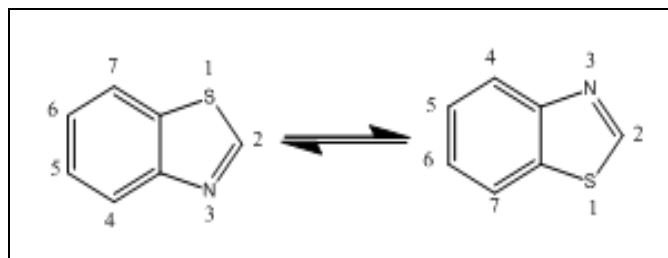
**Appearance:** Pellets large crystal, yellow in colour

**Melting Point:** 2 °C

**Boiling Point:** 227-228 °C at 765 mmHg

**LOGP:** 2.01

**Solubility:** Very soluble in ether, soluble in acetone, alcohol, carbon disulphide and slightly soluble in water.



**FIG. 1: TAUTOMERISM / NUMBERING IN BENZOTHAZOLE**

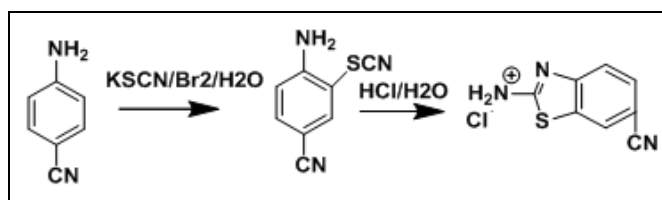
Some of the marketed drugs having benzothiazole derivatives are shown in **Table 1**.

**TABLE 1: MARKETED PREPARATIONS<sup>23</sup> HAVING BENZOTHAZOLE DERIVATIVES**

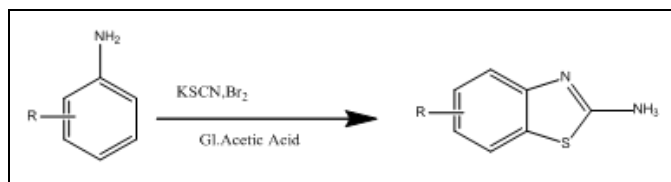
S. no.	Marketed Drug	Company	Use	Structure
1	Pramipexole	Zydus Cadila	Parkinsons disease, restless legs syndrome	
2	Riluzole	Sun Pharmaceuticals	Amyotrophic lateral sclerosis	
3	Ethoxzolamide	Pharmacia, Upjohn	Glaucoma, diuretic, duodenal ulcers	
4	Frentizole		Antiviral, an immunosuppressive agent	
5	Thioflavin T		Amyloid imaging agent	

### Synthesis and Biological Activites:

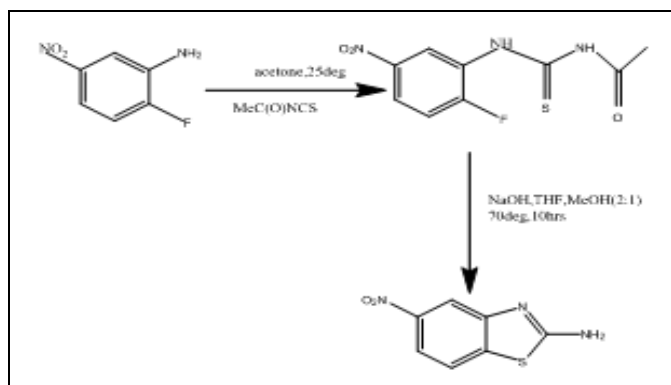
**Several Methods for Synthesis and Pharmacological Properties of Substituted Benzothiazole Reported in the Literature:** Caleta I. et al. reported 2-amino-6-cyanobenzothiazole as antiproliferative agent<sup>24</sup>.



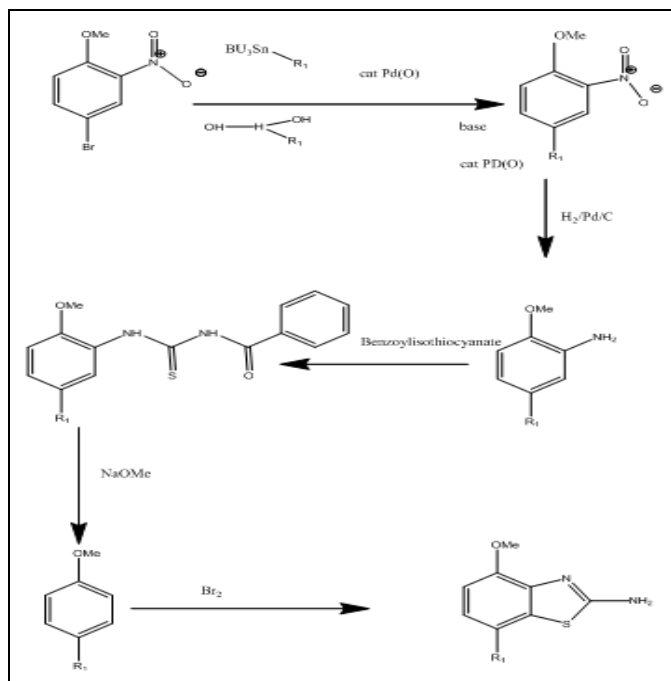
Trapani G. *et al.* reported substituted 2-aminobenzothiazole as anticonvulsant agents<sup>25</sup>.



Yoshida M. *et al.* reported the synthesis and biological evaluation of benzothiazole derivatives as potent antitumor agents<sup>26</sup>.

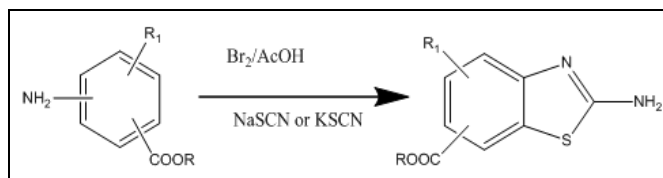


Flohr A. *et al.*, reported 2-amino-4-methoxy-7-substituted benzothiazole as adenosine receptor ligands<sup>27</sup>.



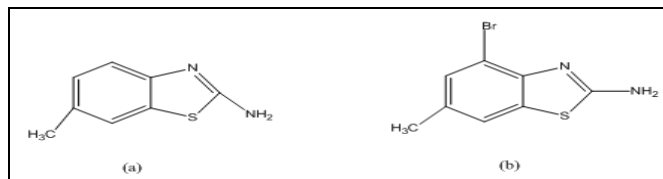
R1 = 3,6-dihydro-2H-pyran-4-yl, 5,6-dihydro-4-H-pyran-3-yl, 5,6-dihydro-4-H-pyran-2-yl, cyclohex-1-enyl, or 1,2,3,6-tetrahydro-pyridin-4-yl

Das J *et al.*, reported substituted 2-aminobenzothiazoles as protein tyrosine kinase inhibitors<sup>28</sup>.

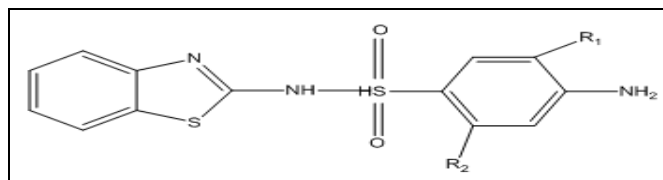


R = alkyl or aryl alkyl, R1 = alkylene or alkenylene

Jung B. Y. *et al.*, reported synthesis and methods for 2-amino-6-methyl-benzothiazole and 2-amino-4-bromo-6-methyl-benzothiazole as antifungal agents<sup>29</sup>.

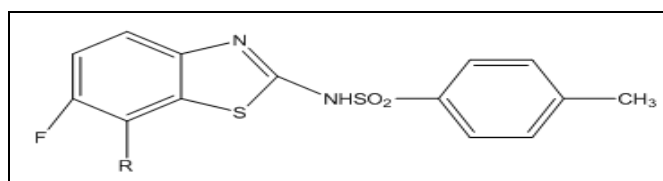


Bhusari K. P. *et al.*, reported substituted 2-(4-aminophenyl sulphonamide) benzothiazoles<sup>30</sup>.



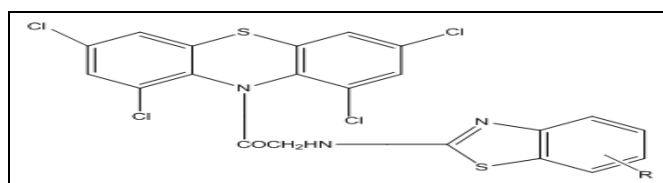
R1 = CH<sub>3</sub>, H, COOH, Cl R2 = H, Br, NO<sub>2</sub>, Cl

Nargund L. V. G. *et al.*, reported 6-Fluoro (N-p-tolyl sulphonamide)-6-fluoro-7-substituted benzothiazoles as antibacterial activity<sup>31</sup>.



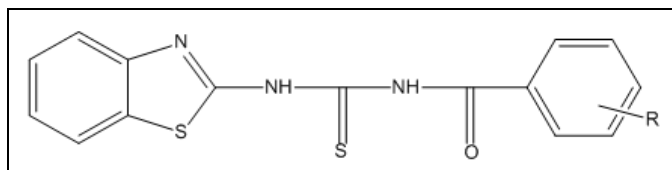
R = HNC<sub>6</sub>H<sub>4</sub>mNO<sub>2</sub>, HNC<sub>6</sub>H<sub>4</sub>pNO<sub>2</sub>, HNC<sub>6</sub>H<sub>4</sub>mCH<sub>3</sub>, HNC<sub>6</sub>H<sub>4</sub>pCH<sub>3</sub>, HNC<sub>6</sub>H<sub>5</sub>, HNC<sub>6</sub>H<sub>5</sub>COOH

Dave A. M. *et al.*, reported the synthesis and antibacterial efficacy of halogenated phenothiazine derivatives by using substituted 2-aminobenzothiazoles<sup>32</sup>.



R=H, 4-Cl, 5-Cl, 6-(Cl)<sub>2</sub>, 6-Br, 4-NO<sub>2</sub>, 5-NO<sub>2</sub>, 6-NO<sub>2</sub>, 5-OCH<sub>3</sub>, 6-OCH<sub>3</sub>, 6-OC<sub>2</sub>H<sub>5</sub>, 6-OC<sub>2</sub>H<sub>5</sub>, 5-OH, 6-OH, 5-CH<sub>3</sub>, 6-CH<sub>3</sub>, 5,6-(CH<sub>3</sub>)<sub>2</sub>, 6-COCH<sub>3</sub>, 6-NHCOCH<sub>3</sub>

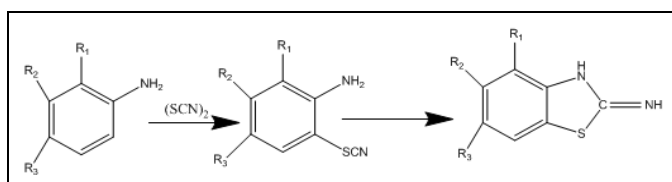
Rana A. et al., reported N-[[[(6-substituted-1,3-benzothiazole-2-yl) amino] carbonothioyl]-2/4-substituted benzamides as anticonvulsant agents <sup>33</sup>.



R=Br, Cl, F, NO<sub>2</sub>, CH<sub>3</sub>, OCH<sub>3</sub>, R<sub>1</sub>=H, 2-Cl, 4-Cl, 4-OCH<sub>3</sub>

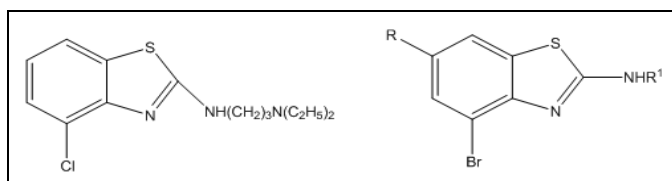
## 2. Synthesis:

Brewster R. Q. and Dains F. B. obtained substituted 2-imino-benzothiazoles by direct thiocyanogenation <sup>34</sup>.



R<sub>1</sub> = NO<sub>2</sub>, H, R<sub>2</sub> = CH<sub>3</sub>, R<sub>3</sub> = H, NO<sub>2</sub>

Elderfield R.C. and Sort F. W. have synthesized substituted benzothiazole <sup>35</sup>.

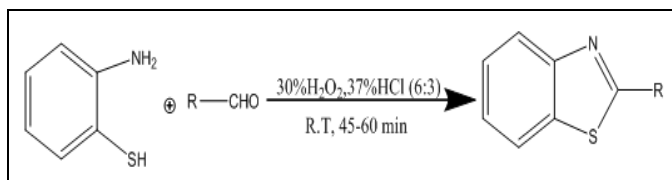


## 3. Some Other Method of Synthesis:

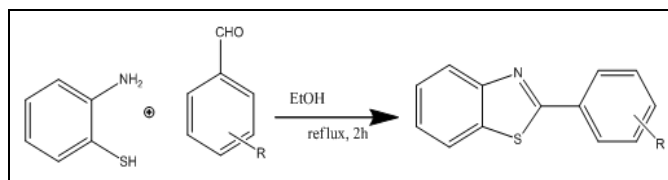
**By Condensation Reactions:** Condensation containing 2-aminothiophenol and aldehydes:-

**Homogeneous Catalysis:** Homogeneous catalysis may be defined as the chemical reaction in which the catalyst and the reactants are in the same phase. The reaction can occur both in the solid and gas phase.

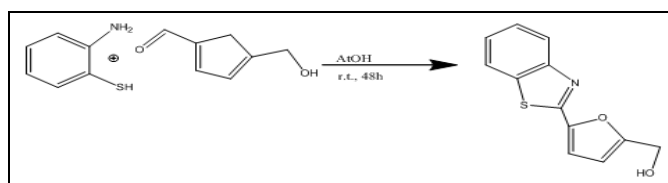
**Acid Catalysed Reaction:** Guo with his fellow members reported the acid catalyzed homogeneous condensation reaction containing 2-aminothiophenol and substituted aldehyde in the presence of H<sub>2</sub>O<sub>2</sub>/HCl in ethanol at room temperature <sup>36</sup>.



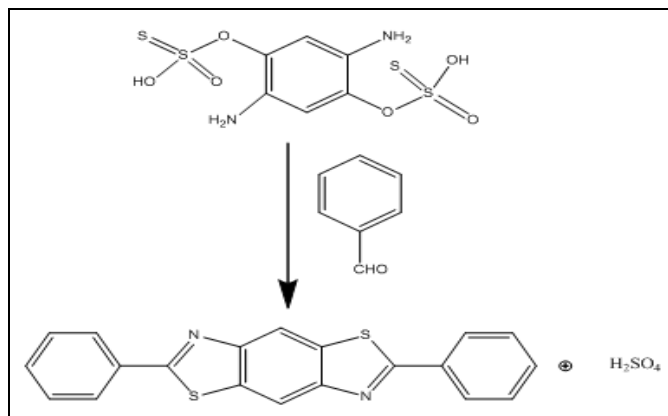
Mortimer synthesizes a series of novel 2-phenyl benzothiazoles by using 2-aminothiophenol and substituted benzaldehyde in ethanol (EtOH) <sup>37</sup>.



In the presence of acetic acid (AcOH) Sattler and his colleagues synthesize [5-(2,3-dihydro-1,3-benzothiazole-2-yl)-oxolon-2-yl]methanol by the condensation of hydroxymethylfurfural (HMF) and 2-aminobenzenethiol <sup>38</sup>.



Perkin et al., synthesizes benzobisthiazole by heating para-phenylene diamine-2,5-di-(thiosulfuric acid) by forming an intermediate benzal derivative which at higher temperature yielded the benzoisothiazole <sup>39</sup>.

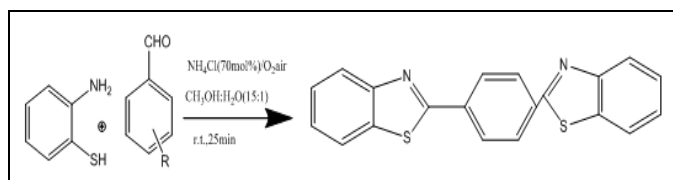
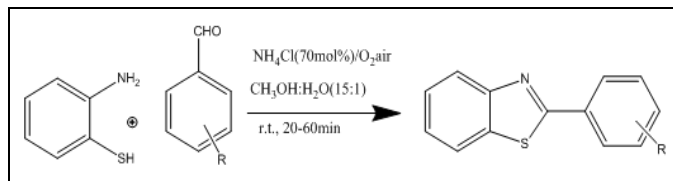


**Base Catalysed Condensation:** Maleki et al., using ammonium chloride as a base develops a method for the synthesis of 2-aryl benzothiazole by the condensation of 2-aminothiophenol with aromatic aldehydes. The solvent system used for this synthesis is methanol/water in the ratio 15:1 v/v at room temperature <sup>40</sup>.

For comparative studies, various authors have chosen different solvents such as ethanol, acetonitrile, chloroform, dichloromethane, and water.

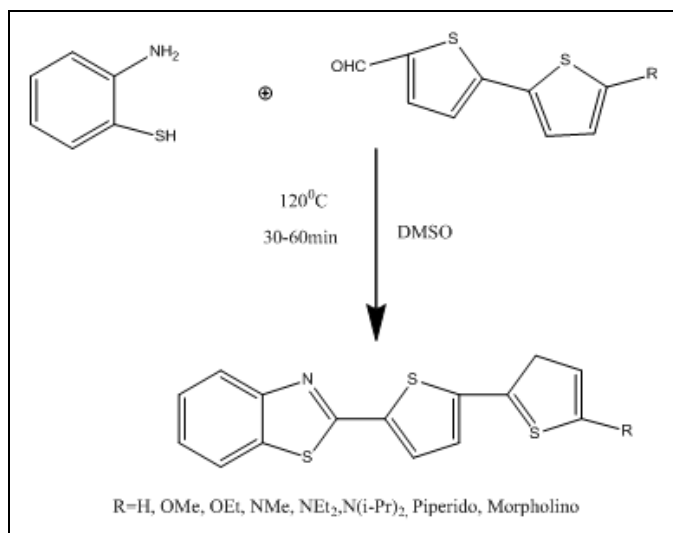
But as far as the studies methanol/water is considered as the best solvent system.

Accordingly, ammonium chloride is used as a base because it is cheap and readily available and is also a metal-free reagent.



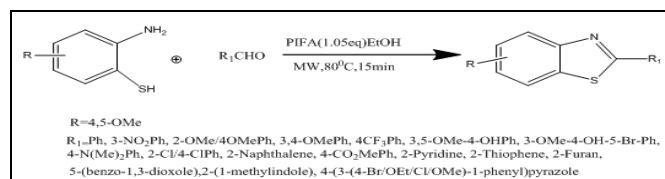
R = H, 3NO<sub>2</sub>, 4-Cl, 4-CN, 2-OH, 4-OH, 3-Br, 2-Me, 4-Me, 4-OMe, 2-OMe, 4-N(Me)<sub>2</sub>

**Solvent Catalysed Condensation:** Batista *et al.*, demonstrated the synthesis of Bithienyl-1-, 3-benzothiazoles, by condensing 2-amino-benzene-thiol and various 5-formyl-5'-alkoxy-bithiophenes or 5-formyl-5', -N, N-dialkylamino-2,2'-bithiophenes and then refluxing with Dimethylsulfoxide (DMSO) FOR 30-60 min<sup>41</sup>.

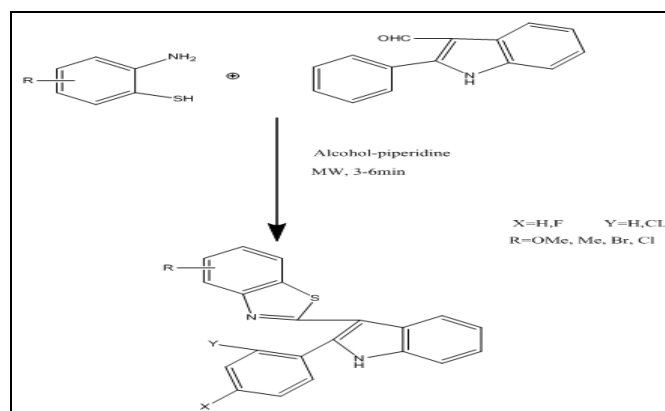


**Microwave Induced Condensation:** Praveen with his colleagues demonstrated microwave induced condensation by using phenyliodonium bis (trifluoroacetate) (PIFA) as an oxidant for cyclocondensation of 2-aminothiophenol / 2-aminophenol using different aldehydes in ethanol at 80 °C, which then gives high yield of benzothiazole and benzoxazole derivatives<sup>42</sup>.

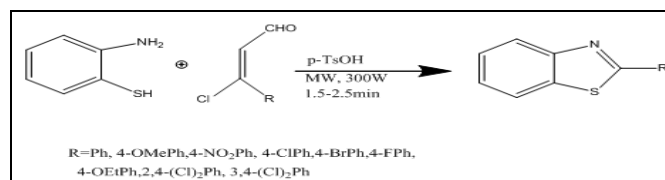
The major advantage is the use of PIFA which works both as Lewis acid and as an oxidant. Also it has wide substrate scope, short reaction time, microwave conditions and a good yield.



Dandia *et al.*, demonstrated the synthesis of benzothiazoles by the condensation of 2-Phenyl-1H-indole-3-carboxaldehyde and 5-substituted -2-aminothiophenols in piperidine or para-toluene sulfonic acid (p-TSA) in ethanol (EtOH) or N, N-dimethylformamide (DMF) under microwave irradiation for 3-6 min at 240W<sup>43</sup>.



Paul *et al.*, finds out an efficient method for the synthesis of 2-aryl benzothiazole by the condensation of 2-aminothiophenol with B-Chlorocinnam aldehydes under microwave irradiation using para-toluene sulfonic acid (p-TSA)<sup>44</sup>. This reaction is meant to be environmentally friendly, fast, simple, general applicability, and accommodating a variety of substitution patterns are the main advantages.



**Heterogeneous Catalysis:** Heterogeneous catalysis is defined as the reaction in which the catalyst and the reactants are in the opposite phase. In these type of reactors, the catalysts are mainly in the solid form while the reactants are in liquid or gas.

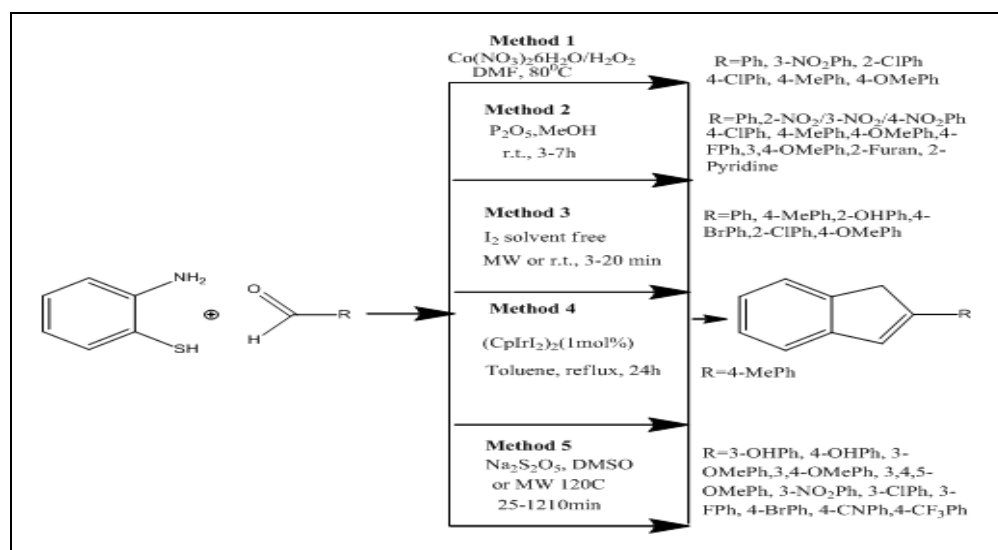
**Acid Catalysed Condensation:** These type of acid catalyzed reaction are followed in these reactions:-

Nalage *et al.*, finds out an efficient method for the synthesis of 2-aryl benzothiazole by condensation of different types of aldehydes and 2-aminothiophenol. This reaction takes place in the presence of phosphorus pentoxide ( $P_2O_5$ ) (act as an acid catalyst) in methanol for 3-5 hrs at room temperature <sup>45</sup>.

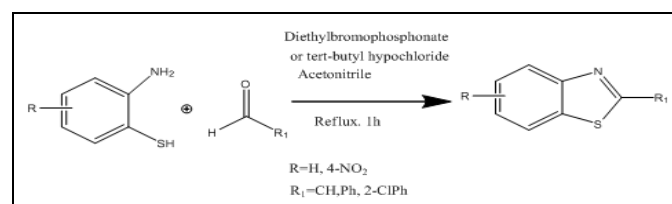
Chandrachood *et al.* finds out an alternative method for the synthesis of 2-aryl substituted benzothiazole using cobalt nitrate ( $Co(NO_3)_2 \cdot 6H_2O$ )/Hydrogen peroxide ( $H_2O_2$ ) as a catalyst. From this, they come to know the importance of temperature, change in reagent amount, change in solvent found the best outcome in Dimethyl-formamide (DMF) <sup>46</sup>.

Moghaddam *et al.*, finds out the most effective and rapid technique which also includes a high yield of the product by using condensation reaction of 2-aminothiophenol with various aldehydes in the presence of iodine as a catalyst. This reaction is a solvent-free reaction <sup>47</sup>. Blacker *et al.*, synthesize 2-(para-tolyl) benzothiazole by transition metal-Ir-catalysed hydrogen transfer reaction of 4-methyl benzaldehyde with 2-aminothiophenol <sup>48</sup>.

Use of Hydrogen peroxide/Cerium ammonium nitrate (CAN) finds out to be the most novel and very efficient reagent for the synthesis of benzothiazole. This reaction was described by Bahrami <sup>49</sup> in which condensation of 2-aminothiophenol with variously substituted aryl aldehydes takes place. This process provides a very high yield product.



A one pot reaction by condensing aldehyde with 2-aminothiophenol or 2-aminophenol for the synthesis of 2-substituted benzothiazole and benzoxazole in the presence of diethyl bromo phosphonate and tert-butyl hypochlorite (t-BuOCl) in acetonitrile (MeCN). This reaction is given by Patil *et al.* <sup>50</sup>



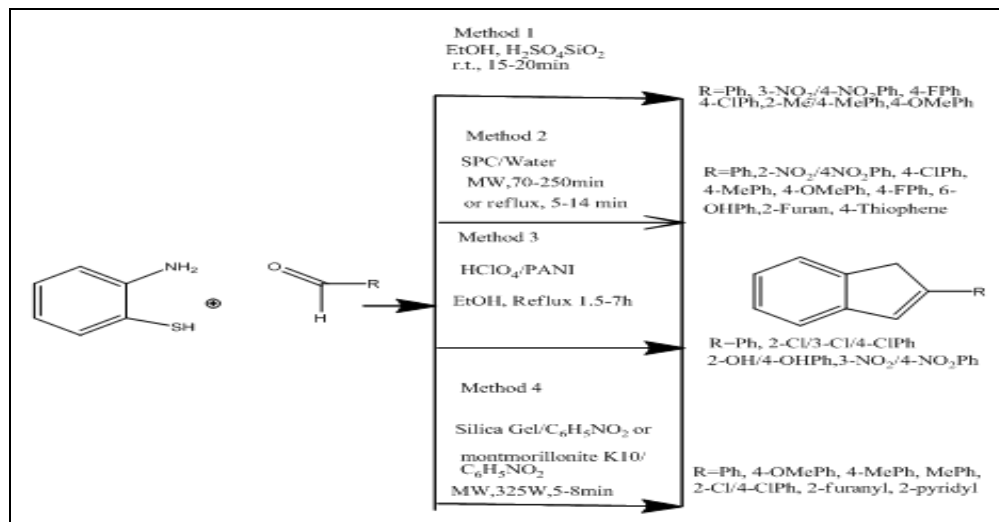
**Solid Support Condensation:** Maleki with his colleagues suggested an efficient method for the synthesis of 2-aryl benzothiazoles through

condensation of various aldehydes and 2-aminothiophenol <sup>51</sup> by using improved catalyst sulphuric acid immobilized on silica gel ( $H_2SO_4 \cdot SiO_2$ ). The  $H_2SO_4 \cdot SiO_2$  used here is the inexpensive, heterogeneous and stable catalyst that has a very high reactivity as compare to unsupported  $H_2SO_4$ . The authors examined various catalysts with different solvents found out that 5 mg of  $H_2SO_4 \cdot SiO_2$  in ethanol is considerably the best.

A second method for the synthesis of benzothiazole derivative was reported by Shokrolahi *et al.*, in which the condensation of 2-aminothiophenol with aldehyde using Sulfonated Porous Carbon (SPC) as a heterogeneous catalyst in water under microwave conditions <sup>52</sup>.

Albeik *et al.*, have suggested the synthesis of 2-substituted benzothiazole efficiently in good yield by the reaction between 2-aminothiophenol and various aldehydes by using perchloric acid doped polyaniline (HClO<sub>4</sub>/PANI) under refluxing ethanol as a catalyst<sup>53</sup>.

Alloum *et al.*, reported the condensation of various aldehydes with 2-aminothiophenol on silica gel/ nitrobenzene or montmorillonite K-10/ nitrobenzene under microwave irradiation which gives 2-aryl benzothiazole in good yield with considerable high purity<sup>54</sup>.

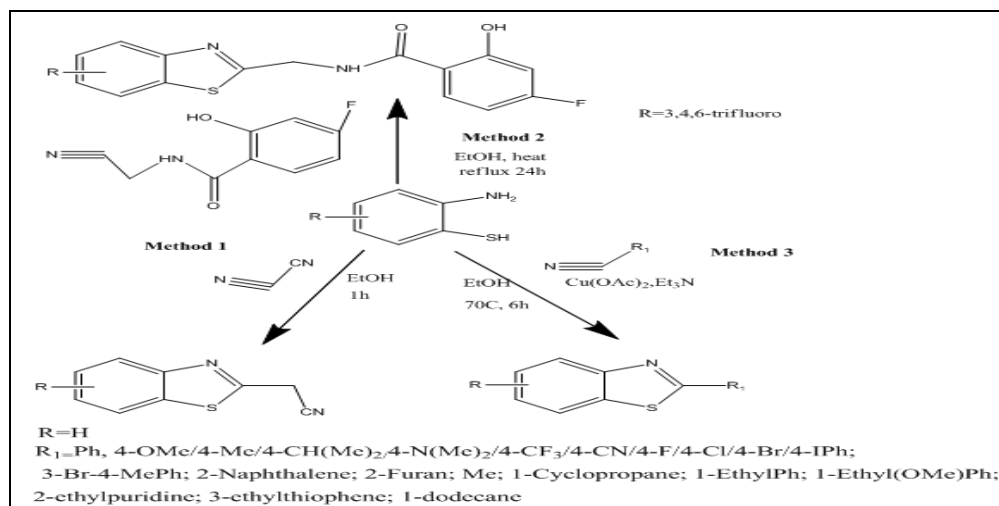


**Condensation of 2-Aminothiophenols with Nitrile:** Mokhier *et al.*, have reported the synthesis of 2-cyanomethyl benzothiazole by the condensation of 2-aminothiophenol and malonodinitrile in the presence of glacial acetic acid as a catalyst<sup>55</sup>.

2-amino-4,5,7-trifluorothiophenol hydrochloride in refluxing ethanol (EtOH) for 24 h was reported by Zandt with his colleagues<sup>56</sup>.

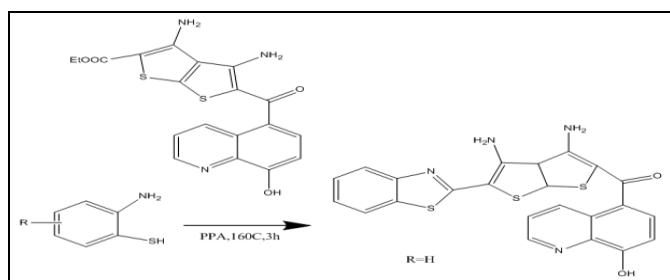
The synthesis of 4-fluoro-2-hydroxy-N(4,5,7-trifluorobenzothiazol-2-ylmethyl)-benzamide using N-cyanomethyl-4-fluoro-2-hydroxy-benzamide and

Sun *et al.*, reported the synthesis of 2-substituted benzothiazole *via* condensation of 2-amino-benzenethiols with a wide range of nitriles containing different functional groups by using copper acetate as a catalyst<sup>57</sup>.

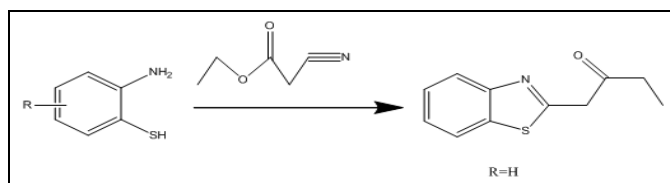


**Condensation of 2-aminothiophenol with Ester:** Khalil *et al.*, have suggested that an amino ester and the selected 2-substituted aromatic amines such as 2-aminothiophenol was condensed to form 2-

substituted benzothiazole. This reaction takes place in the presence of Poly Phosphoric Acid (PPA) at 160 °C for 3 h followed by neutralization with aq ammonia<sup>58</sup>.



Manforni *et al.*, have reported the synthesis of 5-substituted ethyl-2-(benzothiazol-2-yl) acetate by condensing substituted 2-aminothiophenol and ethyl cyanoacetate at 120 °C<sup>59</sup>, which afforded a high yield of products.

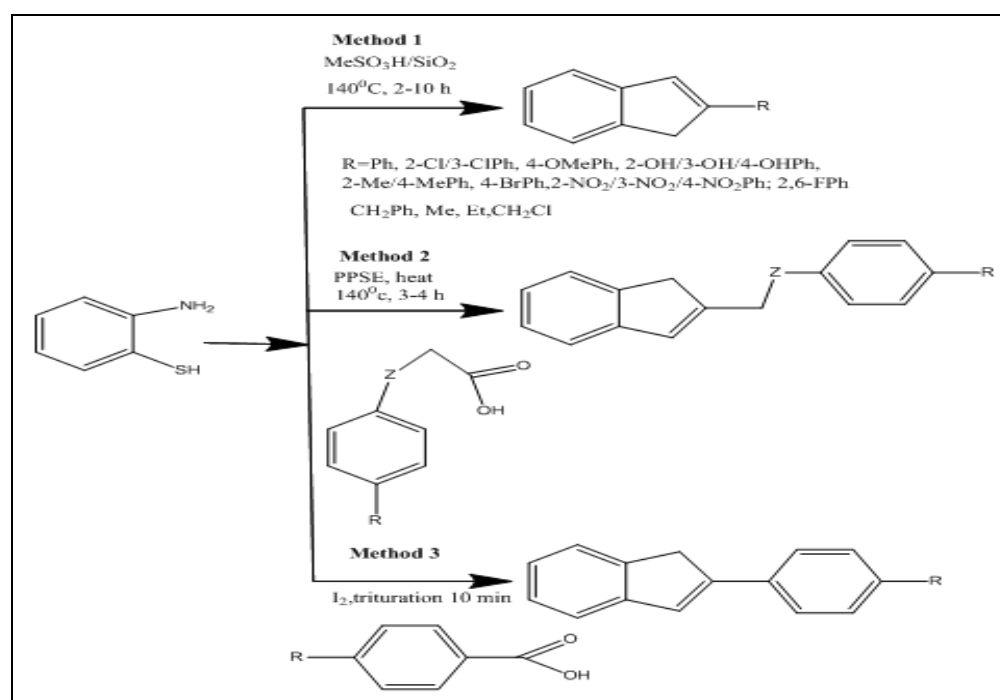


**Condensation of 2-aminothiophenol with Acid:** Sharghi *et al.*, have suggested an efficient, one-pot reaction which produces a high yielding synthesis of 2-substituted benzothiazoles from the 2-

aminothiophenol and different aliphatic or aromatic carboxylic acids in the presence of methane sulfonic acid/silica gel (MeSO<sub>3</sub>H/SiO<sub>2</sub>) at 140 °C for 2-12 h<sup>60</sup>.

Another method for the synthesis of various 2-substituted benzothiazole from 2-aminothiophenols and corresponding carboxylic acid by refluxing in trimethylsilyl polyphosphate ester (PPSE) at various temperature and different time was reported by Yildiz *et al.*<sup>61</sup>

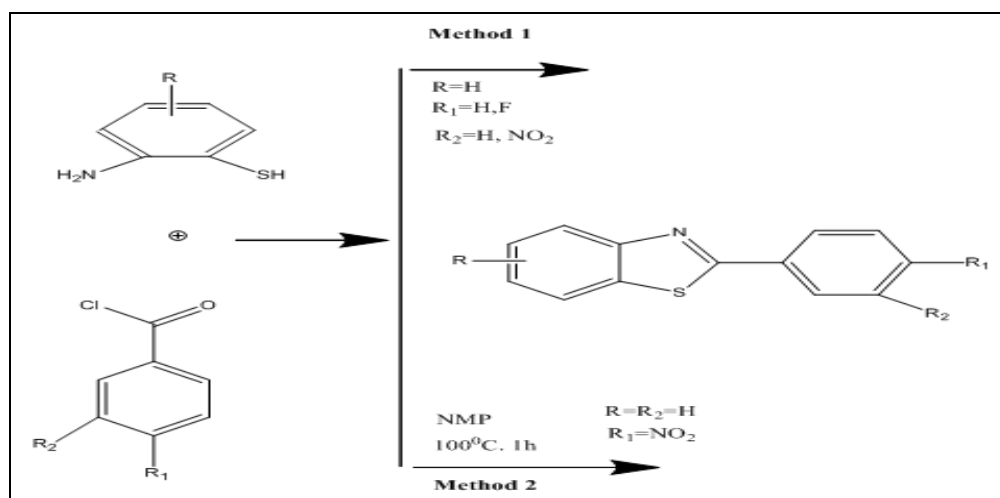
Gupta and his colleagues designed a one-pot, solid phase, solvent-free microwave reaction which includes 2-aminothiophenol and various benzoic acid to synthesize various benzothiazole derivatives in a high yield in the presence of molecular iodine<sup>62</sup>. The advantage of this reaction is that it requires very less amount of iodine and is completed within 10 min. Another advantage is that it requires less cost as compare to PPA and [pmim] Br because no other solvent is required. Therefore it suggests that this reaction is inexpensive, solvent-free and very less time-consuming.



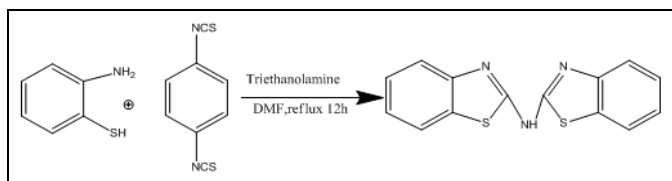
**Condensation with Acyl Chloride:** Nadaf and coworkers developed a novel technique in which they use 1-butylimidazolium tetra fluoroborate ([Hbim]BF<sub>4</sub>) and 1,3-di-nbutylimidazoliumtetra-fluoroborate ([bbim]BF<sub>4</sub>) ionic liquids (ILs) as reaction media for the synthesis of 2-aryl benzothiazoles by condensation of 2-

aminothiophenol and substituted benzoyl chloride<sup>63</sup>. A small change in the above reaction was done by Karlsson *et al.*, in which condensation of 2-aminothiophenol with 4-nitrobenzoyl chloride takes place by applying N-methyl-2-pyrrolidone (NMP) as an oxidant<sup>64</sup>. This reaction takes place at 100 °C for 1 h to give 2-(4-nitrophenyl) benzothiazole.





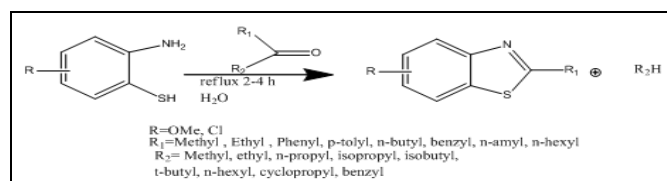
**Condensation with Isothiocyanate:** El-Sharief and coworkers synthesize N,N'-Bis(benzothiazole-2-yl)-benzene-1,4-diamine by the condensation reaction between 1,4-phenylenediisothiocyanate and 2-aminothiophenol using triethanolamine /N,N-dimethylformamide (TEA/DMF) as a reaction media<sup>65</sup>.



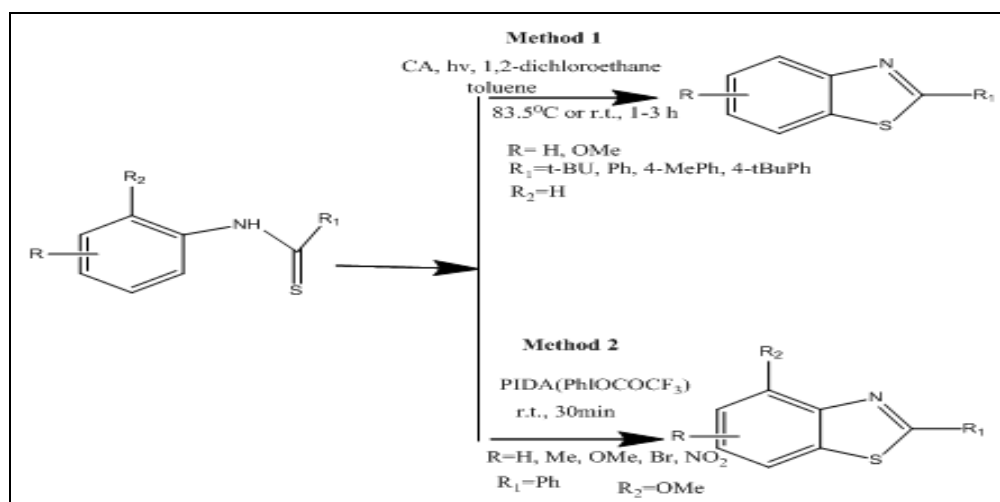
**Condensation of 2-aminothiophenol with ketone:** Elderfield and colleagues describe a method in which reaction takes place between 2-aminothiophenol with various ketones to yield 2,2-disubstituted benzothiazolines, which when pyrolysis yield 2-substituted benzothiazoles<sup>66</sup>.

Kreysa and co-workers have synthesized a novel technique which includes the reaction between 2-

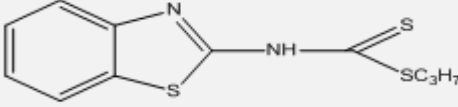
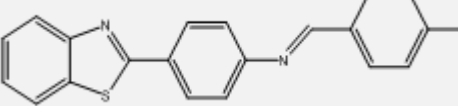
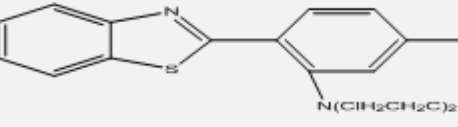
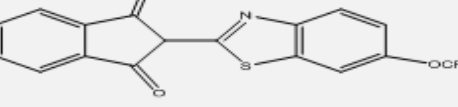
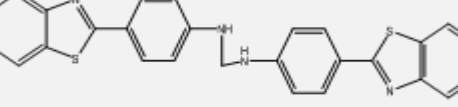
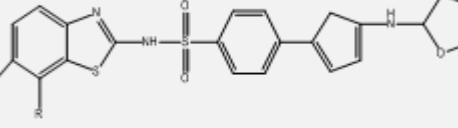
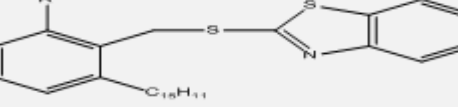
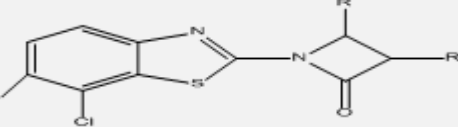
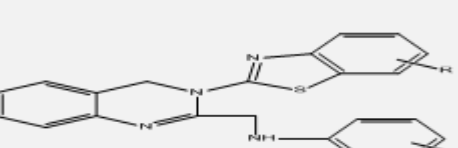
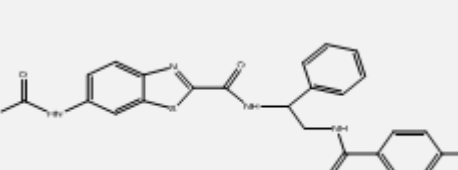
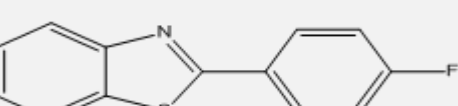
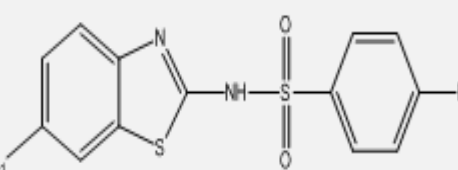
aminobenzenethiol and benzyl methyl ketone to yield 2-methyl benzothiazole<sup>67</sup>.

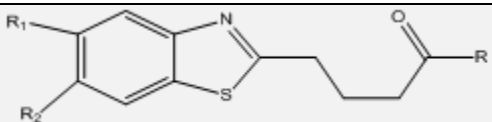
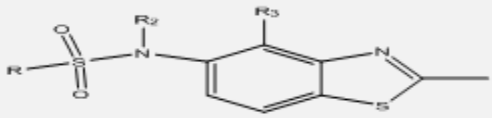
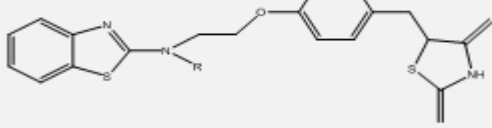
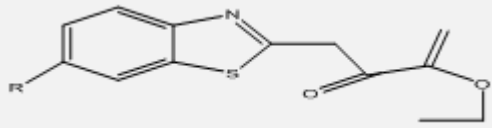
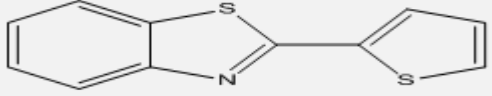
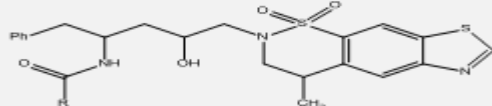
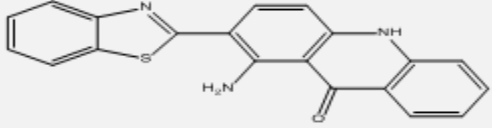
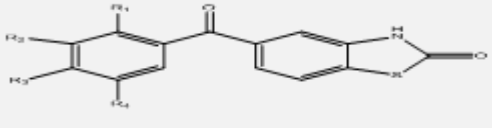


**Cyclization Reactions:** Rey and colleagues define cyclization of thioformanilides propelled by chloranil under irradiation in 1,2-Dichloroethane (DCE) and toluene at 80 °C for the synthesis of 2-substituted benzothiazoles<sup>68</sup>. Another method of cyclization given by Downer *et al.* includes the conversion of thiobenzamides to benzothiazoles through aryl radical cation as a reaction intermediate. This reaction includes phenyliodine (III)bis (trifluoroacetate) (PIFA) in trifluoroethanol or cerium ammonium nitrate (CAN) in aqueous acetonitrile which in turn increases the cyclization to complete within 30 min at room temperature<sup>69</sup>.

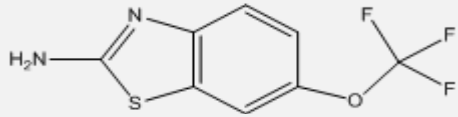
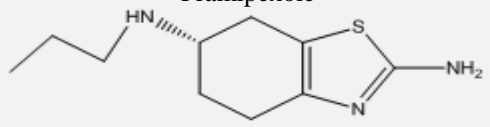
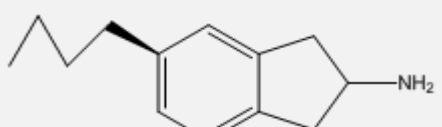


**Biological Activities:**

S. no.	Biological activity	Derivatives	Structure	Activity against
1	Antimicrobial	Pyrimido benzothiazole <sup>70</sup>		<i>E. coli</i> , <i>Enterobacter</i>
		Thiazolidinone <sup>71</sup>		<i>P. mirabilis</i> , <i>S. aureus</i> , <i>S. typhi</i>
2	Anticancer	Aryl substituted benzothiazole <sup>72</sup>		Human cervical cancer cells
		Benzothiazole containing phthalamide <sup>73</sup>		Human carcinoma cells
		Benzothiazole derivative <sup>74</sup>		HL-60 and U-937
3	Anthelmintic	Fluorobenzothiazole comprising sulphonamide pyrazole derivative <sup>75</sup>		Earthworms--
4	Cyclooxygenase inhibitor	2-[(2-alkoxy-6-pentadecylphenyl)methyl]thio-1-H benzothiazole <sup>76</sup>		Cyclooxygenase enzyme-2
5	Antiinflammatory	Azatidine-2-ones and thiazoline-4-ones encompassing benzothiazole derivative <sup>77</sup>		Carrageenan-induced rat hind paw edema method. Diclofenac sodium as standard drug
		3-(6-substituted-1,3-benzothiazole-2-yl)[{94-substituted phenyl}amino]methyl]quinazoline-4(3H)-ones <sup>78</sup>		Inflammatory model in rats. Diclofenac sodium as standard drug
6	MTP inhibition	Triamide derivative based on benzothiazole template <sup>79</sup>		Enterocyte specific microsomal triglyceride transfer protein inhibitor
7	Amyloid imaging agent in Alzheimers disease	F-labeled 2-(4'-fluorophenyl)-1,3-benzothiazoles <sup>80</sup>		Good affinity for amyloid plaque
8	Anti diabetic activity	N-(6-substituted-1,3-benzothiazol-2-yl)benzene sulphonamide derivative <sup>81</sup>		Noninsulin-dependent diabetes mellitus rat model and evaluated for 1-HSD1 and PTP-1B enzymes

		(E)-3-(Benzo[d]thiazol-2-ylamino)phenylprop-2-en-1-ones <sup>82</sup>		Selective inhibitors of 11 $\beta$ -hydroxysteroid dehydrogenase type 1 (11 $\beta$ -HSD1)
		Novel benzothiazole derivative <sup>83</sup>		11-HSD1 using radioimmunoassay method(RIA)
		Benzothiazole derivatives of thiazolidinones <sup>84</sup>		Inhibitory activity of NO production in lipopolysaccharide activated macrophages
		ethyl 2-(6-substituted benzo[d]thiazol-2-ylamino)-2-oxoacetate derivative <sup>85</sup>		Protein tyrosine phosphatase-1B (PTB-1B)
9	Antitubercular	2-(2-(4-aryloxybenzylidene)-hydrazinyl) benzothiazole derivative <sup>86</sup>		<i>Mycobacterium tuberculosis</i>
10	Antiviral	Benzothiazole 71		Protease inhibitor with antiviral activity
11	Anti-leishmanial	(1,3-Benzothiazol-2-yl)amino-9-(10H)-acridinone derivative <sup>87</sup>		<i>In-vitro</i> anti leishmanial activity
12	Antioxidant	Benzophenones containing 1,3-thiazol/5-(2,5-dihydroxybenzoyl)-2(3H)-benzothiazolone <sup>88</sup>		Active against three cell lines ( the cancerous MCF7, noncancerous Htert-HME1, and H9c2 cardio myoblastic cells)

### Benzothiazole in Clinical Trials:

Drugs	Conditions	Phase
Riluzole 	Spinocerebellar ataxia type 2 Inflammation Fatigue Social anxiety disorder PTSD	Phase 3 <sup>89</sup> Phase 4 <sup>90</sup> Phase 2 and 3 <sup>91</sup> Phase 1 <sup>92</sup>
Pramipexole 	Parkinson disease Bipolar disorder Extrapyramidal syndrome Parkinson disease	Phase 4 <sup>93</sup> Phase 4 <sup>94</sup> Early phase 1 <sup>95</sup> Phase 3 <sup>96</sup>
Dexpramipexole 	Major depression disorder	Phase 2 <sup>97</sup>

**CONCLUSION:** The present review article, therefore, highlights the use of benzothiazole derivatives and conclude that they have a marked biological activity. The biological properties of the nucleus include anticancer, anti-inflammatory, anti-diabetic, antiviral, antitubercular, antioxidant.

Hence, this unique molecule must serve as future therapeutic leads to developing various biological agents. It is anticipated that this study would give rise to the design of better molecules which can enhance biological properties and specificity.

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