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A REVIEW ON PHARMACOLOGICAL ACTIVITY AND SYNTHETIC METHODS OF BENZOTHIAZOLE NUCLEUS

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ABSTRACT
Benzothiazole is one of the most important heterocyclic compound, weak base, having varied biological activities and still of great scientific interest now a days. They are widely found in bioorganic and medicinal chemistry with application in drug discovery. Benzothiazole are fused membered rings which contain heterocycles bearing thiazole. Sulphur and nitrogen atoms constitute the core structure of thiazole and many pharmacologically and biologically active compounds. Benzothiazole is among the usually occurring heterocyclic nuclei in many marine as well as natural plant products. Benzothiazole is known to exhibit a wide range of biological properties including anticancer, antimicrobial, and antidiabetic, anticonvulsant, anti-inflammatory, antiviral, antitubercular activities.

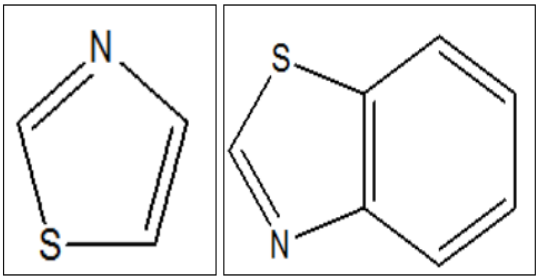
KEYWORDS: Benzothiazole, Pharmacological activities, antimicrobial activity, anti malerial activity, anti bacterial, anti fungal activity.

1.INTRODUCTION

Benzothiazole is a heterocyclic compound containing benzene ring fused with thiazole ring. It is a colorless liquid, with boiling point 227 °C, and soluble in water. Benzothiazole derivatives have attracted sustained interest over the years because of its varied biological activities. Benzothiazole and its derivatives are the most important heterocyclic compounds, which are mutual and vital feature of a diversity of natural products and pharmaceutical agents.[1] The broad spectrum of pharmacological activity in individual benzothiazole derivative indicates that, this series of compounds is of an undisputed interest. The related research and developments in benzothiazole-based medicinal chemistry have become a rapidly developing and increasingly active topic. In bioorganic and medicinal chemistry, 2-aminobenzothiazole derivatives are broadly found with applications in drug discovery and development for the treatment of diabetes, epilepsy, inflammation, ulcer, analgesia, tuberculosis, viral, bacterial infections.[2]

2. Structure of Benzothiozole

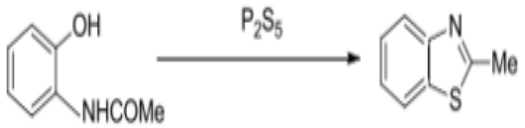
The basic structure of benzothiazole consist of benzene ring fused with d face (4, 5 position) of thiazole. The numbering in thiazole starts from the sulphur atom. **(2).**



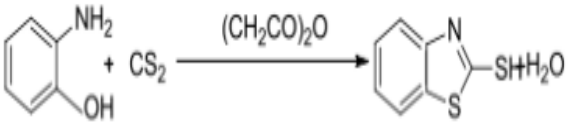
THIAZOLE BENZOTHIAZOLE

3.REACTIONS OF BENZOTHIOZOLE DERIVATIVES.

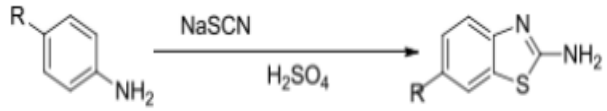
Benzothiazole are also formed by act of phosphoruspentasulfide on O-acylaminophenols[8]



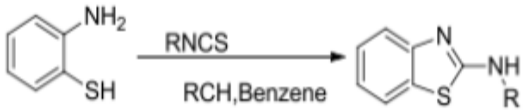
2 mercaptobezothiazole is vulcanisation accelerator be prepared as follows.[8]



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.[9]



Synthesis the cyclizations of isothiocyanates to 2-aminobenzothiazole in presence of benzene which act as a catalyst.[9]



4. SYNTHESIS OF BENZOTHIAZOLES

By Condensation Reaction

1. Condensation of 2-Aminothiophenol with Aldehydes

2-bisthiophene substituted benzothiazole products obtained from the condensation of 2-aminobenzenethiol with 5-aldehyde bisthiophene compounds at the presence of dimethyl sulfoxide (DMSO) under reflflux conditions for 1 h was pointed out by Batista.[10]

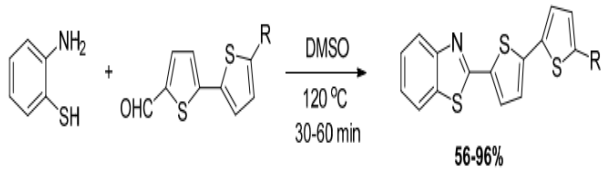


Fig 2: Condensation of 2-aminobenzenethiol with 5-aldehyde bisthiophene compounds.

2. Condensation of 2-aminothiophenol and aldehydes

A series of benzothiazole compounds with different substituents were efficiently synthesized by Guo and co-authors [44] from the condensationof 2-aminothiophenol and aldehydes and their derivatives using a mixture of H2O2/HCl as a catalyst in ethanol at room temperature for 1 h.[11]

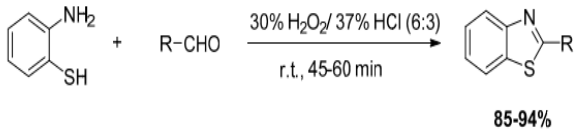


Fig 3: Condensation of 2-aminothiophenol and aldehydes at room tempature.

3. Condensation of 2-aminobenzenethiol and benzaldehyde compound

Kumar et al.found that polystyrene polymer catalysts grafted with iodine acetate could promote the efficient condensation of 2-aminobenzenethiol and benzaldehyde compounds in dichloromethane to synthesize benzothiazole compounds.[12]

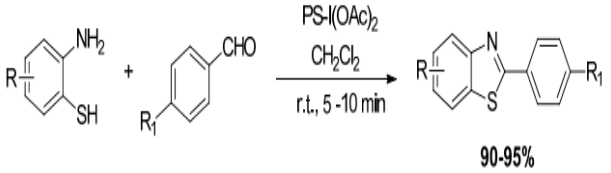


Fig 4:Condensation of 2-aminobenzenethiol and benzaldehyde compound for 5-10min.

4. Condensation of Ortho-aminothiophenol with fatty acids

Reuf et al. have reported that the 2-substituted benzothiazoles were prepared by the condensation reaction of ortho-aminothiophenol with various fatty acids under microwave irradiation for 3-4 min.[13]

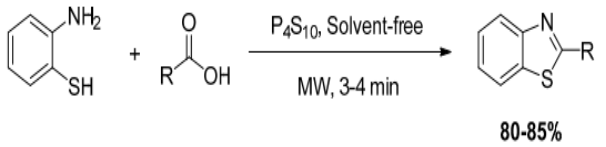


Fig 5: Condensation of Ortho-aminothiophenol with fatty acids.

5. PHARMACOLOGICAL ACTIVITY OF BENZOTHIOZOLE NUCLEUS

Anti-Diabetic Activity: In 2016 Kumar S et.al., synthesized some 2- ((benzothiazole-2 -ylthio) methyl)-5-phenyl-1, 3, 4 oxadiazoles and evaluated their anti-diabetic activity **Fig.6**. In their study, they found that compounds 2-(((6-nitrobenzo [d]thiazol-2-yl) thio) methyl)-5-(4-nitrophenyl)-1, 3, 4-oxadiazole possess excellent anti-diabetic activity.[3]

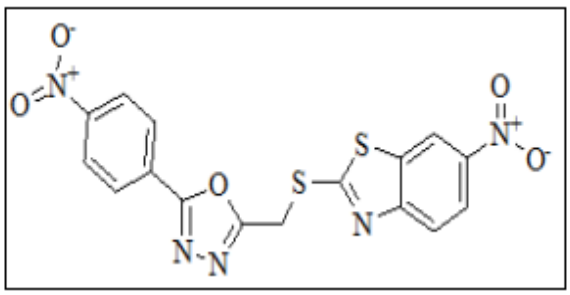


Fig 6: Structure of 2-(((6-nitro benzo[d] thaizol-2-yl)thio)methyl)-5-(4-nitrophenyl)-1,3,4 oxadiazole.

Anti-Diabetic Activity: In 2012 Mariappan G et.al., synthesized some benzothiazole derivative **Fig.7** and evaluated antidiabetic activity and in their study, they found that all synthesized compound possess prominent antidiabetic activity among all compounds, N-(6-chlorobenzoate [d] thiazol-2- yl)-2-morpholinoacetamide found to be most potent compound.[4]

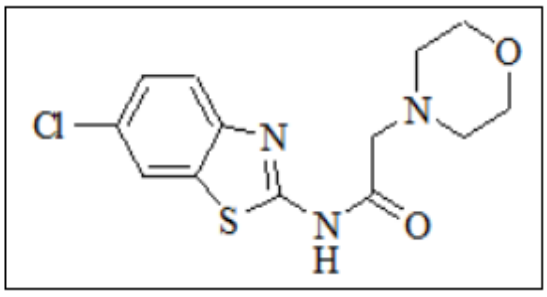
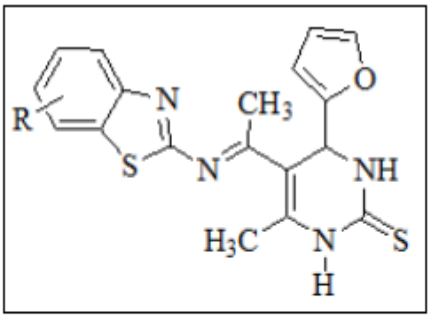


Fig 7: Structure of N-(6-Chlorobenzo [d]thiazol-2-yl)-2-morpholino acetamide.

Anti-Microbial Activity: In 2017 Waghamode KT et al., synthesized some benzothiazole **Fig. 8**.derivatives and evaluated their antibacterial activity against gram positive and gram negative bacterial culture and in their study, they found that all synthesized compound posses good antibacterial activity.[5]



1	H	6	4,6,7- Tri Cl
2	$6OC_2H_5$	7	5- CH_3
3	5-NO_2	8	4- NO_2
4	6 CH_3	9	6- NO_2
5	4 Cl	10	5,6-di- CH_3

Fig. 8: Waghamode KT et al., synthesized benzothiazole derivative.

Antioxidant activity: In 2016 Rosales-Hernandez MC et al, synthesized some benzothiazole derivatives **Fig.9** and evaluated their antioxidant activity. In their study, they found that compound 5-((benzo[d]thiazol2-ylimino) (methyl this) methylamino)-2- hydroxybenzoic acid possess good antioxidant activity.[6]

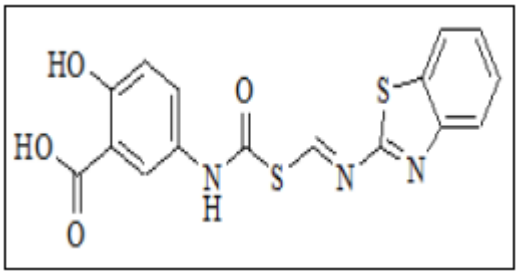


Fig 9: Structure of 5-((benzo[d]thiazol2-ylimino) (methyl this) methylamino)-2- hydroxybenzoic acid.

Antimalarial Activity: In 2016 Sarkar S et al., synthesized some benzothiazole derivative **Fig.10** and evaluated their antimalarial activity. In their study, they found that compound 4-((2 (benzo [d]thiazol-2-yl) hydrazono) methyl) benzene-1, 2- di-ol posses most potent activity.[7]

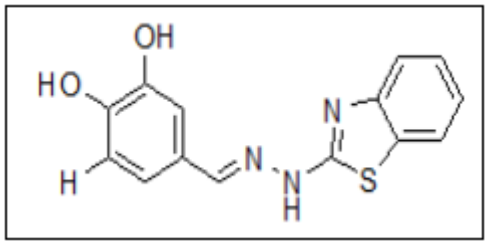
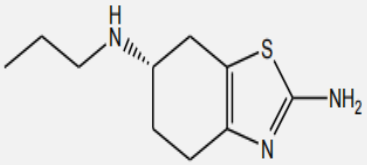
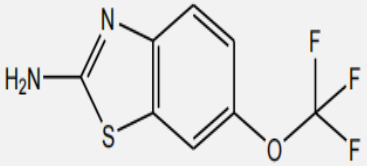
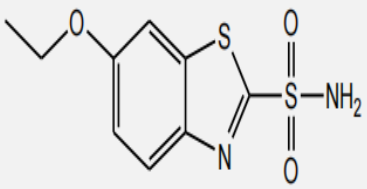


Fig 10: Structure of4-((2-(benzo [d]thiazol-2-yl) hydrazono) methyl) benzene-1, 2- di-ol.

6. MARKETED PREPARATIONS HAVING BENZOTHIAZOLE NUCLEUS[14]

S. no	Marketed drug	Company	Use	Structure
1	Pramiprexole	Zydus cadila	Parkinsons disease, restless legs syndrome	
2	Riluzole	Sun pharmaceuticals	Amyotrophic lateral sclerosis	
3	Ethoxzolamide	Pharmacia, Upjohn, allergan	Glaucoma, diuretic, duodenal ulcers	

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