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A REVIEW ON FLURO-SUBSTITUED BENZOTHIOZOLES: A NEW PROFILE OF BIOLOGICAL ACTIVITIES

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Abstract:
Benzothiazoles are an important class of bioactive & industrially important organic compounds recently; heterocyclic compounds analogues and their derivatives have attracted strong interest in medicinal chemistry due to their biological and pharmacological properties. Heterocyclic compounds analogues and their derivatives have attracted strong interest due to their biological and Pharmacological properties. Benzothiazoles are bicyclic ring system. A number of 2-Aminobenzothiazoles have been studied as central muscle relaxants and found to interfere with glutamate neurotransmission in biochemical, electrophysiological and behavioural experiments Benzothiazoles derivatives have been studied and found to have various chemical reactivity and biological activity. Benzothiazole ring made from thiazole ring fused with benzene ring. Thiazole ring is a five-member ring consists of one nitrogen and one sulphuratom in the ring. The benzothiazole nucleus containing compounds involved in research aimed at evaluating new products that possess biological activities, such as antimicrobial, anticancer, antifungal, anthelmintic, anti-diabetic, and anticancer agents. It is well known that the introduction of fluorine atom into an organic molecule causes dramatic changes in its biological profile, mainly due to high electro negativity of fluorine, the strong carbon-fluorine bond and increased solubility in lipids. These compounds are reported for their antimicrobial and anti-inflammatory, anti tubercular, anthelmintic, antifungal, anti-cancer, anti convulsant activities. Various fluoro substituted benzothiazoles with substituted derivatives they are synthesized by various methods

Keywords: *Benzothiazole, Anti-inflammatory, Antimicrobial, Anthelmintic, Anti convulsant*

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INTRODUCTION:

I.FLUOROBENZENES

The rapid progress of organic Fluorine chemistry since 1950 has been translated as a pathfinder to invent useful biodynamic agents in Medicinal and Biochemistry. The new generation antibiotics like Norfloxacin, Ciprofloxacin, Flufloxacin, Norfloxacin, Ofloxacine and Sparfloxacin which were incorporated with Fluorobenzene moiety proved their efficacy as potent biodynamic molecules. Now a day's vast number of compounds with Fluorobenzene moiety features in diverse areas like antibacterial, antifungal, anti-inflammatory, psychoactive agents, pesticides, herbicides etc.

Based on the above observations we can synthesize some Fluoro benzothiazolo pyrimidine derivatives starting with Fluoro chloroaniline, in hope of getting pharmacological agents with broad spectrum of clinical importance.(*R.Filler J. Fluorine. Chem33, 361-375. (1986).[1]

II. PHARMACOLOGICAL ACTIVITIES OF *FLURO-SUBSTITUED BENZOTHIOZOLES*

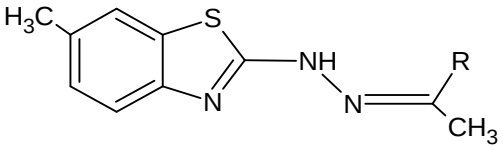
The reasons forever increasing importance of fluorine incorporated bioactive molecules may due to:

- Fluorine being the second smallest substituent next to hydrogen closely mimics Hydrogen.
- The substitution of fluorine by hydrogen increases lipid solubility, which in turn increases the transport and absorption of drug in-vivo.
- The strong electron withdrawing, inductive effect (-I effect) of Fluorine influences stability and reactivity of functional groups that may in turn influence the reactivity of neighbouring reaction centers.
- The replacement of 'Hydrogen' by 'Fluorine' at or near reactive sites causes inhibition of metabolism due to high C-F bond energy. The important pharmacologically active Fluor benzene derivatives are Psychoactive agents, Anticonvulsants,. Antimicrobial .Antidepressants, Cardiovascular agents, Anticancer agents, Non Steroidal anti-inflammatory drugs (NSAID)* L conte. et al., J. Fluorine, chem. 70, 175-179 (1995)[2]sss

III. 2-SUBSTITUTED BENZOTHIAZOLES FOR PHARMACOLOGICAL INTEREST

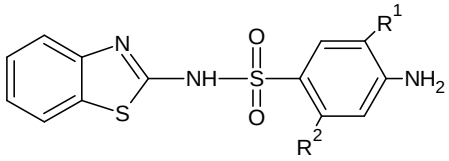
A. ***Antibacterial agent***

*1. Gaurav Alang et al. (2010)*synthesizes seven new derivatives (R_1 to R_7) of benzothiazoles and evaluated their anti-bacterial activity. All the synthesizsed compounds were identified by IR, NMR. The anti-bacterial activity were investigated and appreciate activity were observed.[3]

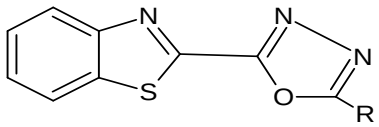


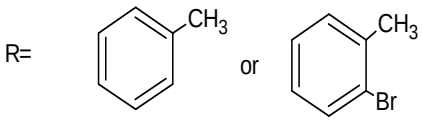
(R= R_1- R_7)
R_1=2'-fluoroacetophenone,
R_2=4'-fluoroacetophenone,
R_3=2'-chloroacetophenone,
R_4 = 4'-chloroacetophenone,
R_5=p-hydroxyacetophenone,
R_6= 2'-hydroxyacetophenone,
R_7= 2, 5-dihydroxyacetophenone

2.*K. P. Bhusari1 et al. (2008),*synthesizes a series of sulphonamide derivatives having benzothiazole nucleus. All the test compounds have been assayed *in vitro* for antibacterial activity against *B. subtilis* and *E. coli*, antifungal activity against *C.* albicans and the anti-mycobacteria activity against H_{37}Rv strain of mycobacterium tuberculosis. The test compounds showed significant antibacterial, antifungal and anti-mycobacterial activity against the microbial strains used.[4]



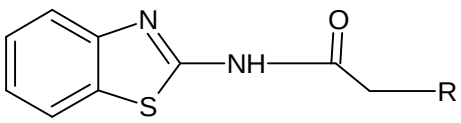
3. *B.Rajeeva et al. (2009),* synthesizes Some new 2-(5-substituted-1,3,4-oxadiazole- 2-yl)1,3-benzothiazole and their anti microbial activity of the synthesized compounds was evaluated by gas diffusion method.[5]



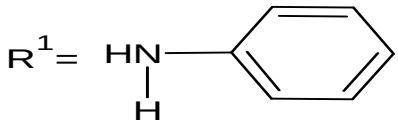


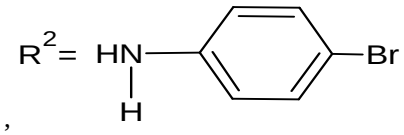
B. ***Antifungal agent:***

1. Hipparagi S. M. et al., (2011), synthesizes a series of various substituted benzothiazole derivatives and most of the compound have shown significant antibacterial and antifungal activity when compared with the standard drug.[6]



R=R^1 or R^2 or R^3





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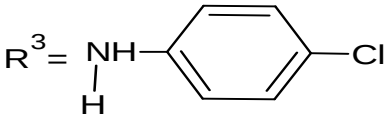
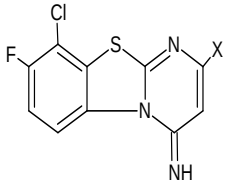
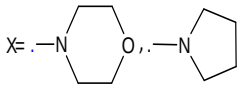


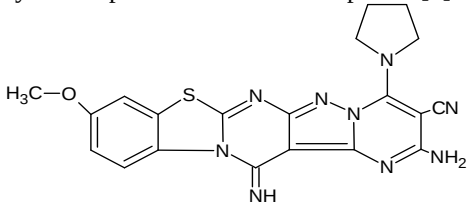
C. ***Anti-inflammatory agent****:*

*1. V. K. Deshmukh et al. (2011),*synthesizes the nucleus 9-chloro-3-cyano-8-fluoro-4-imino-2-methylthio-4-*H* pyrimido [2, 1-*b*] benzothiazole and its 2-substituted derivatives were designed and their toxicity and pharmacological activities were studied with the help of software. Most of the tested compounds revealed significant anti-inflammatory activity, as compare to standard drug Diclofenac sodium.[7]

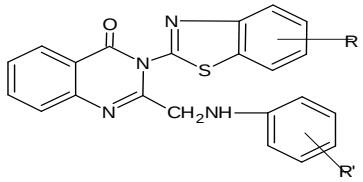




*2. Kamlesh D. Niranjane et al.,(2011),*synthesizes novel derivatives of 2-amino-3-cyano-14-imino-10-methoxy-4-methylthio pyrimido [2,1-b] pyrazolo [4,5-d] pyrimido [2,1-b] benzothiazole were synthesized from starting material 2- amino-6-methoxy benzothiazole and evaluated for their anti-inflammatory activity. It was concluded that some of the compounds showed excellent anti-inflammatory activity as compared with others compound.[8]



*3. Manish Srivastav et al. (2009)***,** synthesizes a series of novel 3-(6-substituted-1, 3-benzothiazole-2-yl)-2-[{(4- substituted phenyl) amino} methyl] quinazolines-4(3*H*)-ones by treating 2-(chloromethyl)-3-(6-substituted-1, 3-benzothiazole-2-yl) quinazoline-4-(3*H*)-one with various substituted amine. Synthesized quinazoline-4-one derivative were investigated for their anti-inflammatory and antibacterial activity. [9]

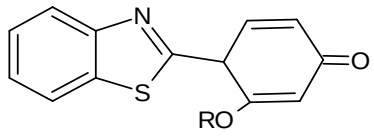


R=CH_3,OCH_3,Cl,F

R'=H,CH_3,OCH_3,Cl

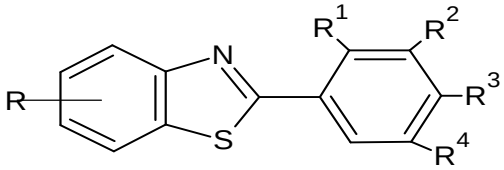
D. Anti-cancer agent:

*1. Geoffrey Wells et al. (2000),*synthesizes a series of new ant tumour agents, the benzothiazole substituted quinol ethers and esters, is reported via the hypervalent iodine mediated oxidation of hydroxylated 2-phenylbenzothiazoles. The products were found to be active in vitro against human colon and breast cancer cell lines with IC50.[10]



R=Et(19%)

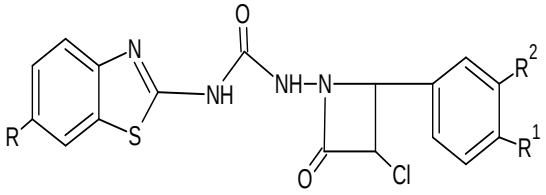
*2. Catriona G. Mortimer et al.(2006),*synthesizes a series of new 2-phenyl benzothiazoles on the basis of the discovery of the potent and selective in vitro antitumor properties of 2-(3,4-dimethoxyphenyl)-5-fluorobenzothiazole. Compounds were evaluated i*n-vitro* in four human cancer cell lines, and compound was found to possess exquisitely potent antiproliferative activity. Potent and selective activity was also observed in the NCI 60 human cancer cell line panel.[11]



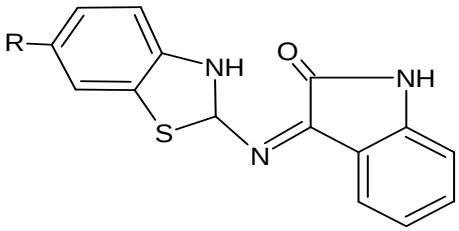
E. ***Anticonvulsant agent***

1. Nadeem Siddiqui et al. (2009), synthesizes a number of new 1-[2-(3,4-disubstituted phenyl)-3-chloro-4-oxoazetidin-1-yl]-3-(6-substituted-1,3-benzothiazol-2-yl) urea compounds and evaluated for their anticonvulsant, hepatotoxic and neurotoxic

properties. The newly synthesized compounds were screened for their anticonvulsant activity.[12]



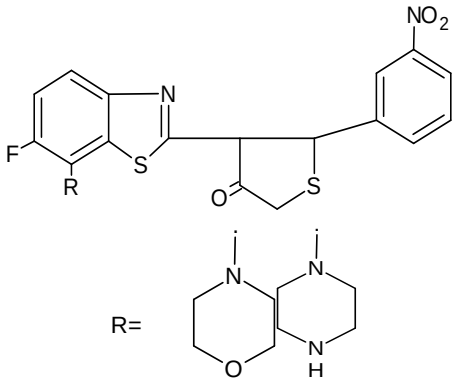
2. Prince P. Sharma et al. (2009), synthesises a series of isatin Schiff's bases and characterized by their spectral data and screened for anticonvulsant and toxicity screening. Some of the investigated compounds showed significant anticonvulsant activity. [13]



R= H, N $(CH_3)_2$, Cl, OCH_3, Br, CH_3, C_2H_5, OC_2H_5, NO_2, F

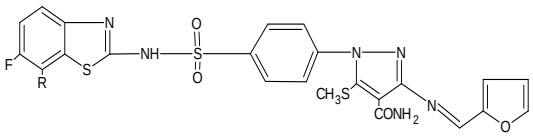
F. ***Anti tubercular agent***

*1. B. S. Sathe et al. (2009***)** synthesizes 2-amino-6-fluoro-7-chlorobenzothiazole by treating 4-fluoro-3-chloroanilline with potassium thiocyanate in presence of glacial acetic acid and bromine. Some compounds.[14]



G. ***Anthelmintic agent:***

*1.Sreenivasa G.M. et al.*synthesizes fluorobenzothiazole comprising sulfonamido pyrazole derivatives and evaluated for their anthelmintic activity. Significant Anthelmintic activities were observed for members of this series.[15]



R = o, m, p - chloro aniline

IV. SUMMARY AND CONCLUSION:

The 2-substituted Benzothiazoles found to possess broad spectrum of pharmacological activity of clinical importance such as Antibacterial agent, Antifungal agent, Anti-inflammatory agent, anticancer agent, Anticonvulsant agent, Anti tubercular agent and Anthelmintic agent. More research has to be done in this direction to get drugs of pharmacological importance to combact the agony of human diseases.

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