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Review on recent progress in antimicrobial potential of substituted-2-aminobenzothiazole derivatives

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ABSTRACT

In recent times fused heterocyclic compounds pursue great attention in the field of medicinal chemistry due to their significant contribution in the biological profile of drug. There is an escalating interest in the chemistry of benzothiazole related compounds. The compounds of benzothiazole have shown significant biological activities with a wide range of practical utility in the medicinal field. In this circumstance, substituted 2-aminobenzothiazole represents an important benzene fused thiazole bicyclic ring scaffolds which have been reported with a wide range of pharmaceutical activities. The present review focuses on the substituted-2-aminobenzothiazoles with potential antimicrobial activities that are now in development.

Keywords: 2-aminobenzothiazole, Antimicrobial activity, Minimum inhibitory concentration.

1. INTRODUCTION

Heterocyclic compounds are very widely distributed in nature and are essential to life in various ways. The chemistry and biological study of heterocyclic compounds has been an interesting field for a long time in medicinal chemistry. Heterocyclic derivatives containing nitrogen and sulphur atom serve as a unique and versatile scaffolds for experimental drug design [1].

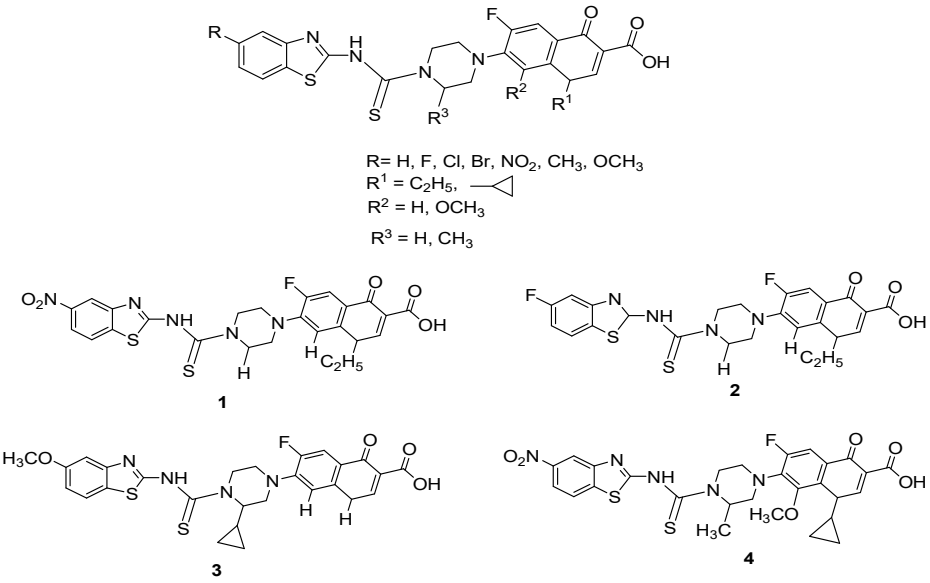
1.1. Importance of benzothiazole nucleus:

Benzothiazole is a privileged bicyclic ring system. It contains a benzene ring fused to a thiazole ring. The small and simple benzothiazole nucleus is present in compounds involved in research aimed at evaluating new products that possess interesting biological activities like anti-tubercular [2], local anesthetic [3], antidiabetic [4], antiulcer [5], antipsychotic [6], Antimicrobial [7], anticancer, anti-inflammatory, analgesic [8], antitubercular [9], Antiviral [10], antioxidant [11]. In addition, the benzothiazole ring is present in various marine or terrestrial natural compounds, which have useful biological activities. Due to their significant pharmalogical profile, the synthesis of various benzothiazole derivatives is of considerable interests.

1.2. Pharmacological profile of 2-aminobenzothiazole:

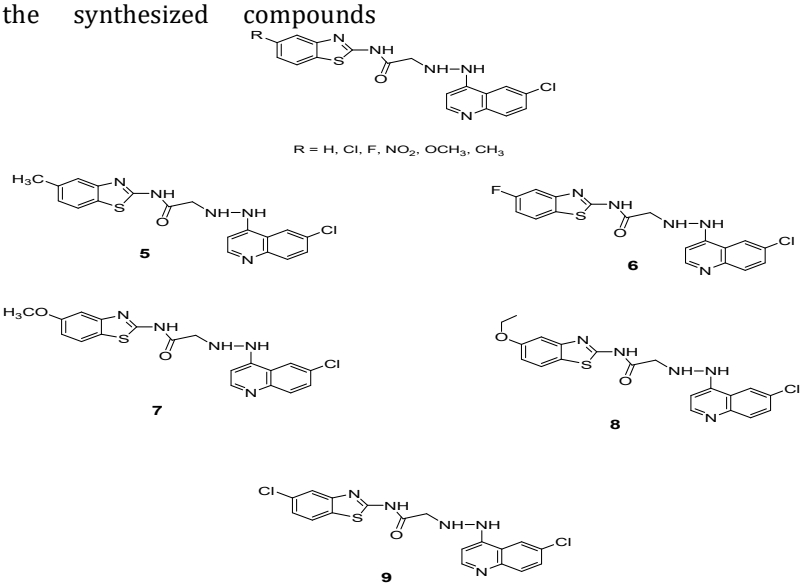
The 2-aminobenzothiazole has shown wide range of pharmacological profile; here in we are presenting the reported antimicrobial activities of various substituted 2-aminobenzothiazole derivatives.

Prabodh Chander Sharma *et al* [12]., synthesized series of novel fluoroquinolone derivatives bearing N-thiomide linkage with 6-substituted- 2-aminobenzothiazole substituents at the C-7 position. The derivatives are characterized by physicochemical and spectral analyses such as ^{1}H NMR and IR. The novel synthesized compounds on in vitro evaluation revealed improved therapeutic effectiveness as compared to the parent drugs. Among the synthesized derivatives, some of the derivatives showed more potent or equipotent antibacterial activities against different strains (S. auerus, B. subtilis, E. coli, P. aeruginosa). But few compounds exhibited outstanding antibacterial activity against Staphylococcus auerus, Escherichia coli, Bacillus subtilis, Pseudomonas aeruginosa bacterial strains. Amongst all the synthesized derivatives 6-nitro substituted-2-amino benzothiazole along with norfloxacin **1** and gatifloxacin **4** showed MIC 05 lg/ml when tested against S. auerus. Moreover, compounds **2, 3** and 4 showed superior MIC (15, 10, and 15 lg/ml respectively) against B. subtilis.



Scheme-1: Synthesis of fluoroquinolone derivatives of 2-amino-6-substituted benzothiazole

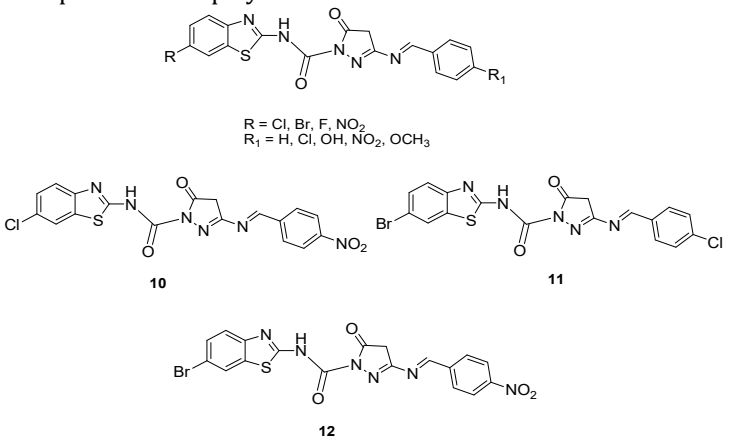
Hitesh D. Patel *et al* [13]., demonstrated a series of N-(benzo[d]thiazol-2-yl)-2-(2-(6-chloroquinolin-4-yl)hydrazinyl) acetamide derivative have been synthesized by sequencing reaction of 2-aminobenzothiazole with chloroacetylchloride, hydrazine hydrate and 4,7-dichloroquinoline.The novel heterocycles were characterized by elemental analyses and various spectroscopic techniques. The synthesized compounds were tested in-vitro antibacterial activity against two Gram-positive and two Gram-negative bacteria with standard drugs. Microbiological results showed that the synthesized compounds possessed a broad spectrum of antibacterial activity against the tested microorganisms. From the antibacterial activity study, Compounds **5**, **6**, **7** and **8** emerged as the most active antibacterial activity against gram positive bacteria. Additionally derivatives **6**, **9** and **8** arose as the majority active antibacterial activity against gram negative bacteria. As a consequence, the newly synthesized derivatives can be used for the development of new antibacterial drugs to cure many disorders caused by the different bacterial species.



Scheme-2: Synthesis of series of N-(benzo[d]thiazol-2-yl)-2-(2-(6-chloroquinolin-4-yl)hydrazinyl) acetamide derivative.

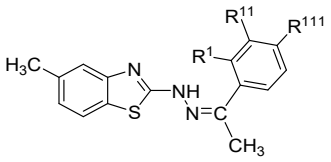
Novel analogs of 3-(4-substituted benzylideneamino)-N-(6-substituted-1,3-benzo[d]thiazol-2-yl)-4,5-dihydro-5-oxo-pyrazole-1-carboxamide were designed and synthesized by reacting 3-amino-N-(6-substituted-1,3-benzo [d]thiazol-2-yl)-4,5-dihydro-5-oxo-pyrazole-1-carboxamide derivatives with p-substituted benzaldehydes carried out by Mahesh B. Palkar *et al* [14]. The structures of all the novel synthesized compounds

were confirmed by the IR, ^{1}H-NMR, ^{13}CNMR, and High Resolution Mass Spectroscopy. The synthesized analogs were evaluated for antibacterial activity. Among the series tested, two compounds **10**, **11** and **12** displayed promising antibacterial activity especially against Staphylococcus aureus (MIC = 3.14 and 1.57 µg/mL) and Bacillus subtilis (MIC = 3.12 and 1.84 µg/mL) respectively. Compound **12** displayed two fold higher activity than the standard drugs against S. aureus with MIC 1.57 µg/mL. Further, these title compounds were also assessed for their cytotoxic activity (IC_{50}) against mammalian Vero cell line using 3-(4,5-dimethylthiazo-2- yl)-2,5-diphenyl-tetrazolium bromide assay, indicating that the compounds exhibit antibacterial activity at non-cytotoxic concentrations.



Scheme - 3: Synthesis of 3-(4-substitutedbenzylideneamino)-N-(6-substituted-1,3-benzo[d] thiazol-2-yl)-4, 5-dihydro-5-oxo-pyrazole-1-carboxamide derivatives.

Alang G *et al* [15]., Carried out the synthesis of five new derivatives of benzothiazoles, all the synthesized compounds were identified by IR and ^{1}H-NMR and antimicrobial activity was performed on the synthesized compounds against *Staphylococcus aureus* (MTCC 737), *Pseudomonas aeruginosa* (MTCC 424), *Escherichia coli* (MTCC1687), and yeast-like fungi *Candida tropicalis*. *p-Toluidine* on treatment with ammonium thiocynate formed 2-benzothiazolamines, which on reaction with hydrazine hydrate formed a hydrazone derivative. Compounds **13** to **17** were synthesized by reacting the hydrazine derivative with different acetophenones. Presence of NO_2, Br, OCH_3, and Cl groups to the substituted benzothiazole enhanced the antibacterial and antifungal activities.



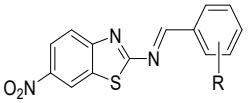
	R	R'	R''
13.	H	NO_2	H
14.	H	H	Br
15.	H	H	OCH_3
16.	Cl	H	Cl
17.	OCH_3	H	OCH_3

Scheme-4: Synthesis of 6-methyl-2(3H)-benzo-1, 3-thiazolyl-1'-ethylidene-2-(o, p- Substituted Acetophenones) Hydrazine Analogs.

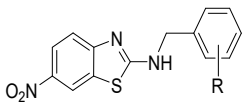
A novel series of Schiff's base derivatives of 6-nitro-2-amino benzothiazoles **18(a-g)** and reduced Schiff's bases **19(a-g)** derivatives were synthesized and evaluated for antibacterial and antifungal activities against *Staphylococcus aureus, Staphylococcus epidermidis, Micrococcus luteus*, *Bacillus cereus, Escherichia coli, Pseudomonas aeruginosa, Klebsiella pneumoniae, Aspergillus niger* and *Candida albicans* by Sushant S. Pande *et al* [16]. Among the synthesized compounds**, 18a**, **18b**, **18d** with para positioned –Cl, –Br, $–NO_2$ substitutents, exhibited most potent *in vitro* antimicrobial activity. This study highlights the importance of Schiff bases with electron withdrawing group's substitution at *para* position in benzothiazoles features responsible for the anti-microbial property.

S. Baluja *et al* [17]., have been synthesized some new fluorine substituted Benzo[d]thiazole derivatives **20(a-c)** and their characterization was done by IR, NMR and mass spectral data. The antibacterial and antifungal activity of these synthesized compounds were done by agar well diffusion method at two different concentrations in DMF against some Gram positive and Gram negative bacteria. It is observed that the synthesized compounds could inhibit both Gram positive bacteria only at higher concentrations and morpholine **20a** substitution is most effective. Against Gram positive bacteria *P. mirabilis*, only two compounds are found to be effective at higher concentrations and piperadine **20c** had no effect against this bacterium. All the compounds exhibited inhibition against fungal strain *A. niger* and morpholine substituent is most effective.

Thus, it is concluded that the synthesized compounds are effective against studied bacterial and fungal strains. *E. coli* is most resistant bacteria.



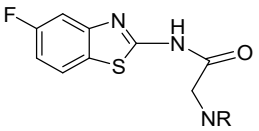
18 (a-g)



19 (a-g)

Compounds	R
a.	p-Cl
b.	p-Br
c.	m-F
d.	p-NO_2
e.	p-OCH_3
f.	p-CH_3
g.	p-OH

Scheme-5: Novel series of Schiff's bases derivatives from 6-nitro-2-amino benzothiazoles and reduced Schiff's bases derivatives.

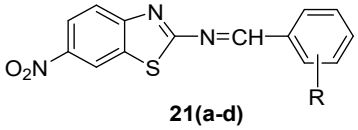


20 (a-c)

Compounds	NR
a.	NC_4H_8O,
b.	$NC_4H_8NC_6H_5$,
c.	NC_5H_{10}

Scheme-6: Synthesis of fluorine substituted Benzo[d]thiazole derivatives.

Amandeep Kaur *et al* [18]., reported the synthesis, spectral studies and biological evaluation of schiff base derivatives of benzothiazole **21(a-d)** for antimicrobial activity moiety. The schiff base derivatives are synthesized by the condensation of 6-nitrobenzo[d]thiazol-2-amine with appropriate aromatic aldehydes afforded N-(2, 5-dimethoxybenzylidene)-6-nitrobenzo[d]thiazol-2-amine. The structures of the compounds were elucidated by spectral studies and screened for antibacterial activity against various strains of Staphylococcus aureus and Escherichia coli and antifungal activity against Candida albicans. The derivatives have shown good activity when compared with standard antibiotic Ampicillin and no activity when compared with standard Fluconazole.

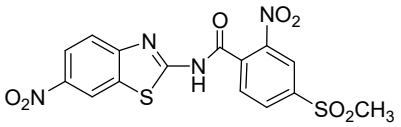


21(a-d)

Compounds	R
a.	H
b.	2, 5-di -OCH_3,
c.	3-NO_2,
d.	4-OCH_3

Scheme-7: Synthesis of Schiff base derivatives N-(2, 5-dimethoxybenzylidene)-6-nitrobenzo[d]thiazol-2-amine.

Manoj Kumar Tyagi *et al* [19]., Synthesized N-(6-methyl benzothiazole-2-yl)-4-(methylsulphonyl) -2-nitrobenzamide **22** is formed by the reaction of 2-amino-6-methyl benzothiazole, and 4-Methylsulfonyl-2-nitrobenzoic acid. Amide synthesis reaction is in the presence of HATU reactions preceded in acceptable yields. These derivatives present a class of compounds that can be used as procedures for the synthesis of new derivatives with useful biological activities such as antimicrobial activity etc.



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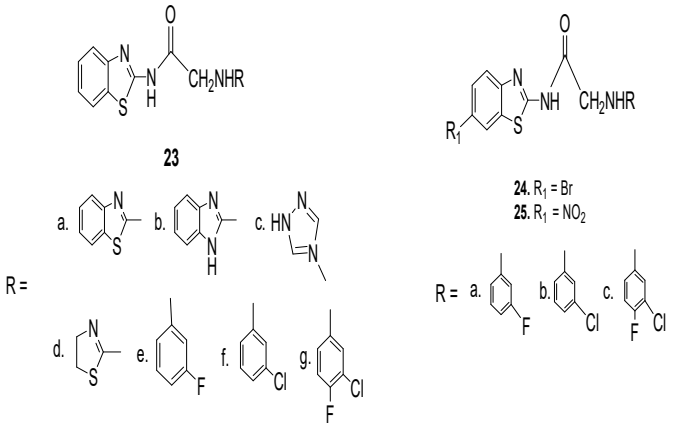
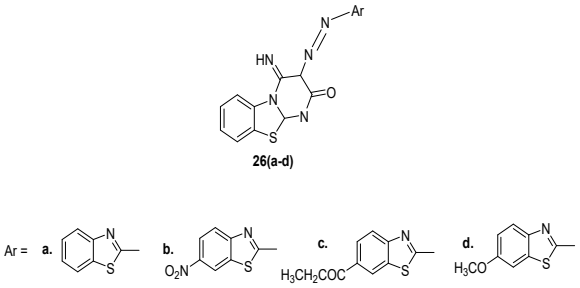
Scheme-8: Synthesis of N-(6-methyl benzothiazole-2-yl)-4-(methylsulphonyl) -2-nitrobenzamide.

Dhamak Kiran Bhausaheb *et al* [20]., synthesized chloroacetamido derivatives of benzothiazole by converting 2-amino benzothiazole to 6 substituted derivatives of 2-amino benzothiazole by nitration and bromination reaction to yield 6-nitro-2-amino benzothiazole **24a** and 6-bromo-2-amino benzothiazole **25(a-c)** respectively, then all the derivatives including 2- amino benzothiazole **23 (a-g)** were further treated with chloroacetyl chloride followed with various heterocyclic and aromatic amines and evaluated for their antifungal activity. The synthesized compounds were confirmed by IR, ^{1}HNMR and Mass spectral data. Synthesized substituted benzothiazole derivatives were investigated for their antifungal activity. It was observed that the new synthesized compounds possessing electron withdrawing group like nitro group at 6th position of benzothiazole nucleus and chloro, fluoro substituted at 3rd position of aromatic amine exhibited moderate antifungal activity when compared to that of other synthesized compounds. It was also observed that the new synthesized compounds possessing electron withdrawing groups like nitro, chloro, fluoro exhibits better activity than the compounds with electron donating groups.



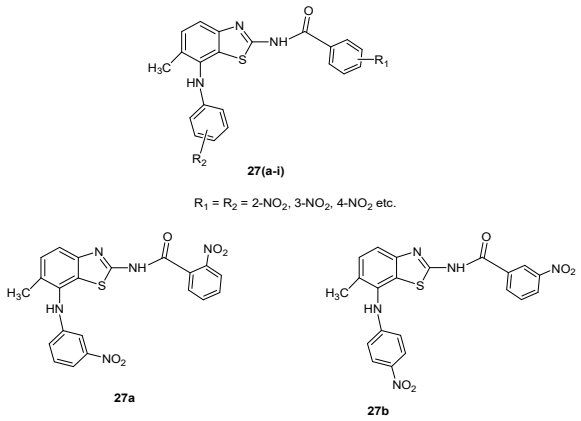
Scheme-9: Synthesis of chloroacetamido derivatives of benzothiazole and substituted benzothiazole.

J Keshavayya *et al* [21]., synthesized novel benzothiazole based azo dyes and its derivatives by diazotization of 2-amino-6-substituted benzothiazoles and coupling with 4-imino-3, 4-dihydro-2H-pyrimido [2,1-b][1,3]benzothiazole-2-one in neutral media under suitable experimental conditions. Synthesized compounds were characterized by various spectroscopic techniques like UV-Visible (electronic spectral), IR, NMR and Mass Spectrometry. The newly synthesized colored compounds are screened for their biological activities like *in vitro* antimicrobial such as antibacterial and antifungal activities. Out of four synthetic derivatives **26(a-d), 26b** and **26d** shows fine anti-bacterial activity and compounds **26b** and **26c** shows anti-fungal activity.



Scheme-10: Synthesis of azo derivatives of 2-amino benzothiazole.

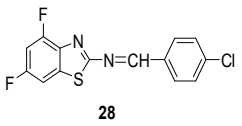
Akhilesh Gupta [22] have synthesized novel C-6 methyl substituted benzothiazole derivatives by reaction of methyl-chloro substituted aniline with potassium thiocyanate under temperature control and presence of bromine in glacial acetic acid and ammonia. Substituted nitrobenzamides then synthesized by condensation of C-6 methyl, 7-chloro and 2-amino substituted benzothiazole with 2, (3 or 4)-nitrobenzoylchloride acid in presence of dry pyridine and acetone.These novel compounds were screened for antifungal activity against C. albicans. The antifungal studies showed that compound **27a** and **27b** showed potent activity.



Scheme-11: Synthesis of chloroacetamido derivatives of benzothiazole and substituted benzothiazole.

Novel benzothiazole Schiff bases namely N-(4-chlorobenzylidene)-4,6-difluorobenzothiazole-2-amine; 4,6-difluoro-N-(4-nitrobenzylidene)benzothiazol-2-amine and N-((1H-indol-3-yl)methylene)-4,6-difluorobenzothiazole-2-amine have been synthesized from condensation reaction of 4,6-difluoro-2-amino benzothiazole with different aromatic aldehydes like 4-chlorobenzaldehyde, 4-nitrobenzaldehyde and 1H-indole-3-cardaldehyde by Keyur D Bhatt *et al* [23]. The structure of Schiff bases have been confirmed by various physicochemical and spectral analyses. Schiff bases have been screened for antimicrobial activity against bacteria and fungi by using MIC determination. *In vitro* antibacterial and antifungal activity of ligands were assayed against gram positive (*S. Aureus, B.Subtilis*), gram negative bacteria (*S. Marcescens, E. coli*) and *Rhizopus sp.* and *A. Niger*. The standard drugs ketoconazole and ciprofloxacin were used to screen antimicrobial activity. In this study, these Schiff base derivatives **28**, **29** and **30** are found active

antimicrobial compounds. Among the three Schiff base tested, **28**and **30** exhibited the promising antimicrobial activity and **29** is most active against both the fungal strains.



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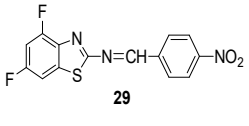

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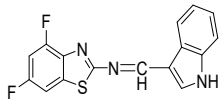

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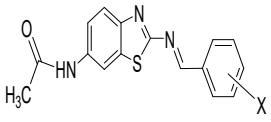
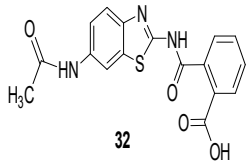
Scheme-12:Synthesis of Novel benzothiazole Schiff bases N-(4-chlorobenzylidene)-4,6-difluorobenzothiazole-2-amine; 4,6-difluoro-N-(4-nitrobenzylidene)benzothiazol-2-amine and N-((1H-indol-3-yl)methylene)-4,6-difluorobenzothiazole-2-amine.

Abhay kumar verma *et al* [24]., investigated the synthesis benzothiazole Schiff's bases **31(a-d**) from para amino acetanilide, then it is subjected to treatment with various substituted aromatic aldehydes to get the corresponding**)** followed by treatment with phallic anhydride to form 2-(6-acetamidobenzo[d]thiazol-2- ylcarbamoyl)benzoic acid **32**. The structures of synthesized compounds were confirmed by various spectroscopic methods such as IR, ^{1}H NMR and mass spectroscopy. The products were evaluated for their antibacterial activity. Some of the compounds exhibited potent activity when compared with the standards.



31(a-d)



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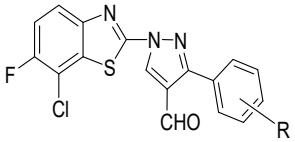
X = P-Chloro, P-Methoxy, 3-Nitro, P-Methyl

Synthesis-13: Synthesis of benzothiazole Schiff's bases and 2-(6-acetamidobenzo[d]thiazol-2- ylcarbamoyl) benzoic acid.

Sachin G. Lokapure *et al* [25]., described the preparation of 3-aryl-1-(7-chloro-6-fluoro-1-benzothiazole-2yl) pyrazole derivative were prepared from the schiff's bases of aromatic ketones with dimethyl formamide and phosphorous oxychloride undergo cyclization forming pyrazole derivatives and undergo formylation on to the pyrazole ring. The structure of the synthesized compounds have been established on the bases of spectral (IR, ^{1}HNMR and Mass) Properties and their elemental analyses. Further, these were tested for anti-bacterial activity against S.aureus ATCC 29213, E.coli ATCC 25922, Pseudomonas aeruginosa MTCC 741 and anti-fungal activity against Aspergilus niger ATCC 1015, Candida albicans ATCC 9025 in cup plate method. Evaluation of the compound revealed moderate to good antimicrobial activity. The obtained results revealed that the nature of substituent and substitution pattern on the benzene ring may have a considerable impact on the antibacterial and antifungal activities of the synthesized compounds have particular importance, a nitro group has a considerable impact on antibacterial and antifungal activity. The antimicrobial data revealed that the synthesized compound was superior to the other derivatives.



R= C_6H_5, 3-OCH_3-C_6H_4, $2NH_2$-C_6H_4, 4-Br-C_6H_4, 4-Cl-C_6H_4, 2-Cl-C_6H_4

Synthesis-14: Synthesis of 3-aryl-1-(7-chloro-6-fluoro-1-benzothiazole-2yl)pyrazole derivatives.

2. CONCLUSION

The 2-aminobenzothiazole and its analogs research elucidated in this review furnish the antimicrobial activities. A further modification in its main nucleus provides more efficient derivatives with more potent therapeutic efficacy.This review illustrates many efficient protocols for the synthesis and evaluation of various antimicrobial activity of Benzothiazole nucleus substituted with different aromatic, heterocyclic and other groups.

Acknowledgement

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3. REFERENCES

1. Achson A, *An. 3rd ed.,* Willy-Intersciences India, 2009.
2. Nayeem N, Denny G, Synthesis of some Mannich bases from sulphonamides and benzothiazole derivatives and evaluation of their anti tubercular activity and anti microbial activity, **Der Pharma Chemica.** 2012; 4; 1277-82,
3. Geronikaki A, Vicini P, Dabarakis N, Lagunin A, Poroikov V, Dearden J, *et al*. Evaluation of the local anaesthetic activity of 3-aminobenzo [d] isothiazole derivatives using the rat sciatic

nerve model, **European Journal of Medicinal chemistry**. 2009; 44: 473-481,

4. Mariappan G, Prabhat P, Sutharson L, Banerjee J, Patangia U, Nath S, Synthesis and antidiabetic evaluation of benzothiazole derivatives, **Journal of Korean Chemical Society**. 2012; 56: 251-256.
5. Pareek D, Chaudhary M, Pareek P K, Kant R, Ojha K G, Pareek R, *et al*. Synthesis of some bioactive 4-thiazolidinone derivatives incorporating benzothiazole moiety, **Der Chemica Sinica.** 2010; 1: 22-35.
6. Arora P, Das S, Ranawat M, Arora N, Gupta M, Synthesis and biological evaluation of some novel chromene-2-one derivatives for antipsychotic activity, **Journal of Chemical Pharmaceutical Research**, 2010; 2: 317-323.
7. Wada J, Suzuki T, Iwasaki M, Miyamatsu H, Ueno S, Shimizu M, A new nonsteroidal anti-inflammatory agents, 2- substituted 5-or 6-benzothiazole acetic acids and their derivatives. **Journal of Medicinal Chemistry**, 1973; *16*: 930-934.
8. Majo V J, Prabhakaran, J, Mann J J, Dileep Kumar J S, An efficient palladium catalyzed synthesis of 2-arylbenzothiazoles. **Tetrahedron Letters**. 2003; *44*: 8535-8537.
9. Bhusari, KP, Khedekar PB, Umathe SN, Bahekar RH, Raghu Ram Rao A, Synthesis and antitubercular activity of some substituted 2-(4-aminophenyl sulfonamido) benzothiazoles. **Indian Journal of Heterocyclic Chemistry**, 2000; 9: 213-216.
10. Akerfeldt S. Studies on the in vivo antiviral effects of benzothiazole derivatives against various influenza A_2 strains. Journal of Medicinal Chemistry, 1970, 13: 1012-1013.
11. Pustoshnaya LS, Pustoshnyi VP, Mmazitova AK, Khamaev VK, Davydov EY, Zaikov GE, Antioxidant effect of triazinone derivatives in thermal oxidation of polyisoprene. **Polymer Degradation Stabilization**, 2000; 70: 39-41.
12. Prabodh Chander Sharma, Ankit Jain, Mohammad Shahar Yar, Rakesh Pahwa , Jasbir Singh, Preeti Chanalia, Novel fluoroquinolone derivatives bearing N-thiomide linkage with 6-substituted-2- aminobenzothiazoles, Synthesis and antibacterial evaluation, **Arabian Journal of Chemistry**, 2017;10: S568–S575.
13. Manoj N. Bhoi, Mayuri A. Borad, Hitesh B. Parmar and Hitesh D. Patel, Synthesis and Characterization of novel N-(benzo[d]thiazol-2-yl)-2-(2-(6-chloroquinolin-4-yl)hydrazinyl)acetamide derivatives containing Quinoline linkage as potent antibacterial agents, **International Letters of Chemistry, Physics and Astronomy**, 2015; 53:114-121.
14. Mahesh B. Palkar, Aniket Patil, Girish A. Hampannavar , Mahamadhanif S. Shaikh Harun M. Patel, Ashish M. Kanhed, Mange Ram Yadav, Rajshekhar V. Karpoormath, Design, synthesis and QSAR studies of 2-amino benzo[d]thiazolyl substituted pyrazol-5-ones: novel class of promising antibacterial agents. **Medicinal Chemistry Research**, 2017.
15. Alang G, Kaur G, Kaur R, Singh A, Tiwari R, Synthesis, Characterization, and Biological Evaluation of certain 6-methyl-2(3H)-benzo-1, 3-thiazolyl-1'-ethylidene-2-(o, p-Substituted Acetophenones) Hydrazine Analogs, **Journal of Young Pharma**, 2010; 2(4): 394-398.
16. Padmavathi P. Prabhu, Sushant S. Pande, Rahul N. Dubey, and Panneer Selvam T, Syed Aamir, **Journal of Pharmaceutical Research**, 2012; 5(7): 3830-3833.
17. Baluja S, Bhesaniya K, Talaviya R, Synthesis and biological activities of fluoro substituted benzothiazole derivatives, **International Journal of Chemical Studies**, 2013; 1(3): 28-33.
18. Rajinder Kumar, Uday Kalidhar, Amandeep Kaur and Puneet Kaur, Synthesis, Spectral Studies and Biological Evaluation of Schiff Base Derivatives of Benzothiazole for Antimicrobial Activity. **Research Journal of Pharmaceutical, Biological and C hemical Sciences**, 2012; 3(4): 847-854.
19. Manoj Kumar Tyagi, Aakash Kumar, Anuj Garg, Synthesis Characterization and Antimicrobial Studies of New Novel Derivatives of 2-Amino- 6-Methylbenzothiazole, International **Journal of Innovative Research in Science, Engineering and Technology**, 2017; 6(3): 4239-4244.
20. Dhamak Kiran Bhausaheb, Gaware Vinayak, Madhukar, Somwanshi Sachin Balkrishna, **International journal of pharmacy and pharmaceutical research-Human**, 2015; 3(1): 112-124.
21. Maliyappa MR, Keshavayya J, Shoukat Ali RA, Harisha S, Synthesis, Characterization, Solvatochromic and Biological studies of novel Benzothiazole based azo dyes, **Journal of Chemical and Pharmaceutical Sciences**, 2018; 1: 10-15.

22. Akhilesh Gupta, Antifungal Activity of Novel C-6 Methyl Substituted Benzothiazole Derivatives against Candida albicans, **Journal of Cosmetology & Trichology**, 2018; 4(2): 1000134.
23. Surbhi V Upadhyay, Raksha V Zala and Keyur D Bhatt, Synthesis, Characterization and Biological Screening of Schiff bases derived from 4, 6-difluoro-2-amino Benzothiazole, **Medicinal & Analytical Chemistry International Journal**, 2020; 4(1); 000157.
24. Abhay kumar verma, Synthesis, Characterization and antibacterial activity of benzothiazole derivatives, **International Journal of Pharmaceutical Research and Development**, 2014; 6(8); 080-085.
25. Sachin G. Lokapure, Shivakumar B and Kalyane NV, Synthesis of novel 1-(7-chloro-6-fluoro-1-benzothiazole-2yl)-3-aryl pyrazole as potential antimicrobial agents, **Der Pharmacia Lettre**, 2013; 5(3); 21-26.