IJBPAS, June, 2024, 13(6): 2994-3008

ISSN: 2277–4998

International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS)

'A Bridge Between Laboratory and Reader'

www.ijbpas.com

SCOPE OF BENZOTHIAZOLE SCAFFOLD: A REVIEW

KAUR H[1], KAUR G[2], LATA S[3], BHANDARI DD[4*] AND SINGH G[5]

[1, 2, 3]ASBASJSM College of Pharmacy, Bela (Ropar), 140111 Punjab, India

[4]University Institute of Pharmaceutical Sciences, Panjab University, Chandigarh 160014 India

[5]IET Bhaddal Technical Campus, Mianpur (Ropar), 140108 Punjab, India

***Corresponding Author: Dr. Divya Dhawal Bhandari; E Mail: bhandaridivya3320@gmail.com**

Received 15th April 2023; Revised 8th June 2023; Accepted 25th Sept. 2023; Available online 1st June 2024

https://doi.org/10.31032/IJBPAS/2024/13.6.8123

ABSTRACT

Reviewing, the issue of antimicrobial resistance, which is one of the most urgent topic of public health today, chemists are working towards the development of medicinal agents of therapeutic importance. The development of resistance such as multi-drug resistance towards various antibiotics or adopted by bacterial strains possesses a challenge to the scientific community for the innovation of new remedies. Thus, there is an ample need to develop newer and more effective drug molecules with high safety profiles. The main objective is to find synthetic chemical compounds that can be fused with a number of heterocyclic to generate medicinal compounds of therapeutic importance. One of such compound is Benzothiazole consisting of a benzene ring fused with the *d* face (4, 5 position) of thiazole. The benzothiazole moiety possesses various biological activities thus representing as an active biological compound with diverse properties. This review focuses on already available benzothiazole nucleus containing drugs and their action and also about the various modifications that can be done on this moiety.

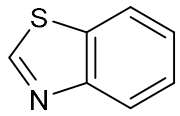
Keywords: Benzothiazole, Pharmacology, Anti-cancer, Anti diabetic, Anti tubercular

INTRODUCTION

Benzothiazole (BTA) and its derivatives are among the utmost essential heterocyclic compounds; originated in natural commodities (blackberries, black tea, and green tea) and pharmaceutical drugs (Riluzole, Ethoxolamide). The development of medicinal chemistry containing benzothiazole nucleus has been rapid

because it is highly active moiety. Molecular designing by incorporation of various biologically active heterocyclic pharmacophores into one single molecule could be a source of benefit for emerging hybrid molecules with interesting and versatile biological potential. Benzothiazole chemicals are frequently used in medical care to address a wide variety of illnesses with good results. It covers a novel class of beneficial compounds offered to exert a widespread series of biological activities. Benzothiazole acknowledged as a biologically active compound for many years but it is still a scientific research topic due to its varying properties. BTA and analogues have structural diversity for the production of new medicinal drugs possessing a large number of pharmacological properties. Its applications as anticancer, antibacterial, antifungal, anti-inflammatory, analgesic, antioxidant, anticonvulsant, anti-tuberculosis, antidiabetic, antimalarial and other therapeutic agents.

New ideas are stimulating research towards benzothiazole-containing drugs that are less toxic, and more effective for diseases that are getting diagnosed. The newer research is focused towards finding the biological aspects of Benzothiazole thus looking for synthetic procedure as well as pharmacological activities of benzothiazole **[1-4]**. Benzothiazole is a class of sulfur-containing heterocyclic compounds which contains a benzene ring fused with a thiazole ring. The basic structure of benzothiazole consists of a benzene ring fused with the *d* face (4, 5 position) of thiazole **[4]**.



benzo[*d*]thiazole

The benzothiazole ring system formerly originated in several marines and terrestrial natural compounds, which are widely used in imaging reagents, enzyme inhibitors, antioxidants, anti-inflammatory agents, vulcanization accelerators, fluorescence materials, and plant growth regulators. It is also used in electroluminescent devices due to its biological and high pharmaceutical activity **[5-8]**.

Benzothiazole is a privileged bicyclic ring system containing a benzene ring fused with a thiazole ring containing electron-rich heteroatoms, nitrogen and sulphur, which fascinate significant interest from researchers to design the drug due to its effective therapeutic activities. **[9-13]** such as analgesic **[14]**, anti-inflammatory **[15-19]**, antidiabetic **[20]**, and anti-cancer [21]. Benzothiazole derivatives are used to treat various diseases like local cerebral ischemia, cancer **[22]** and neurological diseases and a number of 2- amino benzothiazole were intensively studied as central muscle relaxants. 2-

Aminobenzothiazoles exhibit high antiviral activity **[23-31]**, which plays a vital role in this period of the global COVID-19 pandemic.

Its application involves dye intermediates **[32]**, fungicides **[33]** photographic inducers **[34]**, appetite suppressants **[35]**, β-amyloid plaque imaging agents **[36]**, and plant protectors **[37]** as given in **Figure 1**.

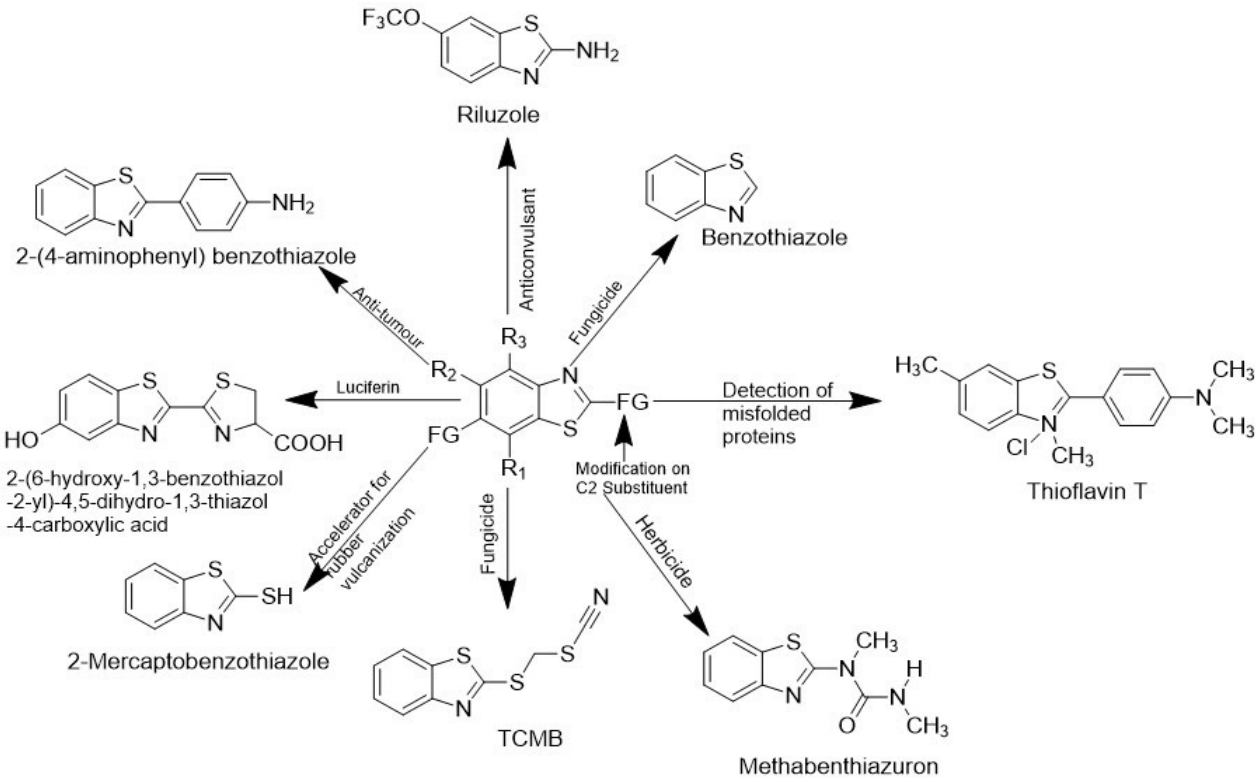
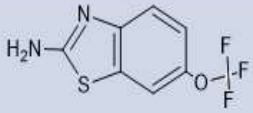
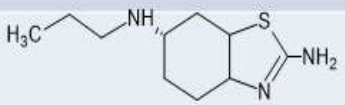
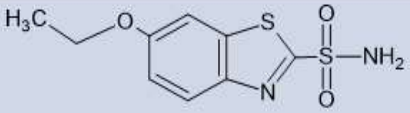
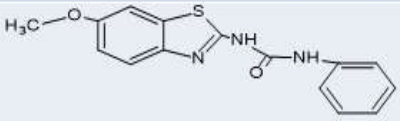
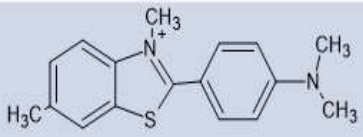


Figure 1: Various applications of Benzothiazole nucleus containing drugs

Benzothiazole is a flavoured chemical produced by the fungi *Aspergillus clavatus* and *Polyporus frondosus*, and is found in tea leaves and cranberries **[38]**. It is also found in natural resources on sea or land. Its molecules are used in several arenas of chemistry, in polymer chemistry **[39]**, pharmaceuticals **[40]**, and silver photography. The salts of Benzothiazole derivatives are also used as sensitive dyes **[41, 42]**. Sulfide bonds that arise from benzothiazole derivatives of elastomeric unsaturated polymers are used in several molecules; such as tire manufacturing **[43]** and the resulting elastic material is cross-linked (MBT/BTSH) as a rubber accelerator. Some Marketed drugs of Benzothiazole and their uses are given in **Table 1**.

Table 1: Some marketed drugs of Benzothiazole and its uses

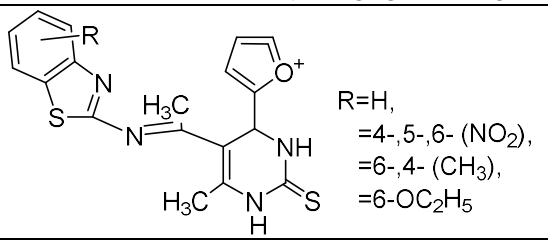
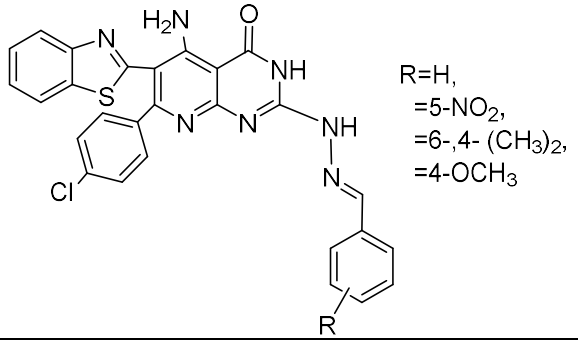
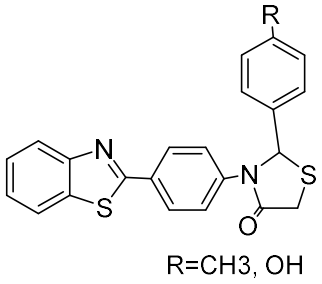
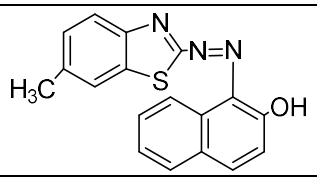
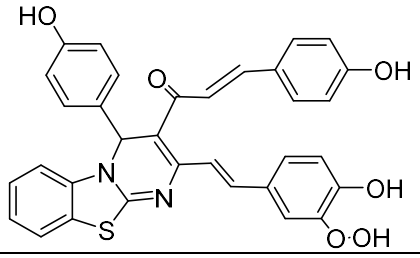
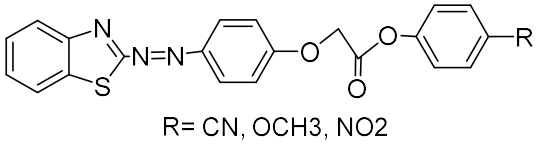
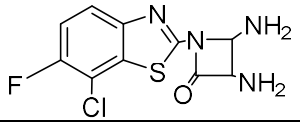
S.No	Marketed drug	Company	Use	Structure
1.	RILUZOLE	Sun pharmaceuticals	Amyotrophic lateral sclerosis	
2.	Pramiprexole	Zydus cadila	Parkinsons disease, restless legs syndrome	
3.	Ethoxzolamide	Pharmacia, Upjohn, allergen	Glaucoma, diuretic, duodenal ulcers	
4.	Frentizole	Not Available	Antiviral, immunosuppressive agent	
5.	Thioflavin T	Not Available	Amyloid imaging agent	

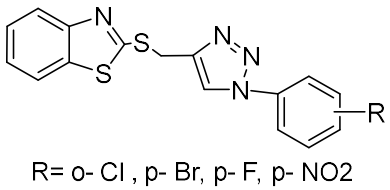
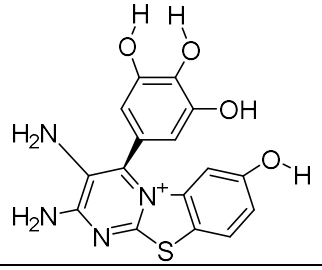
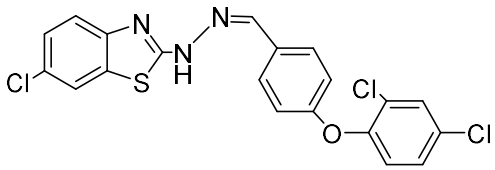
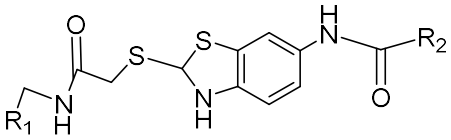
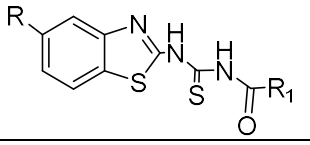
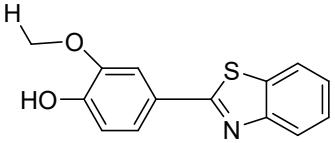
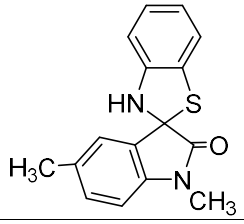
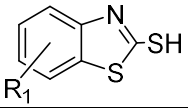
PHARMACOLOGICAL ACTIONS OF BENZOTHIAZOLE AND ITS DERIVATIVES

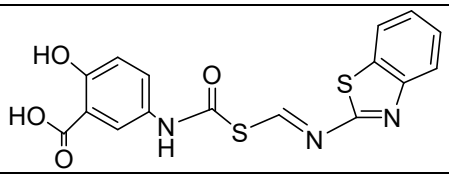
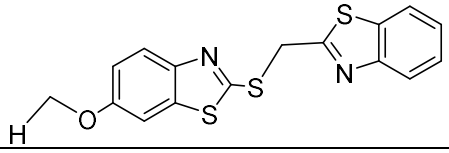
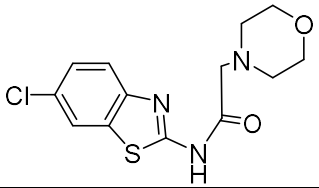
Benzothiazole and its derivatives (BTA) are essential pharmacophores. This moiety has attracted considerable attention as its structure is familiar with other drugs of medicinal chemistry that are helpful to cure a range of clinical disorders **[46]**.

Many medicines are used in the treatment of antimicrobial infections that prevent the growth and suppress the multiplication of bacteria **[47]**. When it occurs for longer duration and over the time make this worse or increasing the risk of disease spread and making infection harder to treat, then antimicrobial resistance occurs and it becomes common and serious **[48]**. Antimicrobial therapy has progressed a lot and noteworthy threat. A number of scientists researched on the benzothiazole derivatives as potent antimicrobials, anti-inflammatory agents, anti-tubercular, anticancer, anti-oxidants and anti-diabetic some of which are mentioned in **Table 2 [49-66]**.

Table 2: Pharmacological profile of Benzothiazole derivatives

S. No.	Name of Scientist	Compound/Derivatives	Type of compound	Activity
ANTIMICROBIAL PROFILE				
1	**E Waghamode KT *et al.***		**Substituted benzothiazole derivatives**	**Showed excellent activity against Gram Positive and Gram Negative Bacterial strains**
2	**Lavanya P *et. al.***		**Substituted benzothiazole pyrimidine derivatives**	**Showed excellent antibacterial and antifungal activity**
3	**Mr. Singh *et. al.***		**Substituted benzthiazolidine derivatives**	**Showed the most active antimicrobial activity on gram positive and gram negative bacteria.**
4	**Bele *et. al.***		**Benzothiazole derivatives**	**Showed antimicrobial activity on various species of bacteria.**
5	**P.K. Sahu *et. al.***		**4-(4-hydroxyl phenyl)-4*H*-pyrimido-[2,1-*b*]-[1,3] benzothiazole**	**Showed antimicrobial activity on gram negative and gram positive**
6	**H.R. Tomi *et. al.***		**Oxazole and benzothiazole derivatives**	**Benzothiazole derivatives showed active antimicrobial activity than oxazole derivatives.**
ANTIINFLAMMATORY PROFILE				
	Gurupadayya *et. al.*		**Benzothiazole derivatives**	**Showed excellent anti-inflammatory effect by using diclofenac**

				sodium as a standard drug.
	Shafi *et. al.*		**2-Mercapt benzothiazole triazole derivatives**	**Showed optimum anti-inflammatory effect.**
	Kashinath DV *et. al.*		**Pyrimid-[2, 1-*b*] [1, 3] benzthiazole**	**Showed optimum anti-inflammatory activity.**
ANTITUBERCULAR PROFILE				
	Telvekar and *et. al.*		**2-(2-(4arylxybenzyldene) hydrzinyl) benzothiazoles**	**Showed excellent anti-tubercular activity.**
ANTICANCER PROFILE				
	Wang and *et. al*.		**Benzothiazolethiol derivatives**	**Evaluated as ant proliferative properties in mainly two cells (HepG2 and MCF -7)**
	Leal KZ *et. al.*		**2-Benzothiazole hydrzones derivatives**	**Showed excellent anticancer profile.**
ANTIOXIDANT PROFILE				
	Amin S. *et. al.*		**Benzothiazole derivative**	**Showed potential antioxidant profile.**
	Guzel *et. al.*		**3*H*-Spir [benzothia zole indol]-20 -(10*H*)ones**	**Showed more scavenging activities against (ABTS+) radicles and DPPH.**
	Cressier D. *et. al.*		**Thiadiazolo derived benzothiazoles**	**Showed good antioxidant activity**

	Rosales Hernandez MC *et. al.*		**Benzothiazole derivatives**	**Showed higher level of antioxidant activity.**
ANTIDIABETIC ACTIVITY				
	Sasson S *et. al.*		**Benzothiazole derivatives**	**Showed excellent antidiabetic activity**
	Mariappan G *et. al.*		***N*-(6-chlorbenzoat[d] thiazol2-yl)-2-morpholinocetamide**	**Showed excellent antidiabetic activity**

CONCLUSION

Benzothiazole and analogues played a vital role in medicinal chemistry as it is a versatile heterocyclic scaffold having remarkable therapeutic importance due to the presence of sulphur and nitrogen heteroatom in a fused bicyclic rings of 6 & 5-membered. Benzothiazole hybrid molecules are not only synthetically important as building molecules for designing development but also possess a wide variety of pharmacological activities. The biological profiles of the new BTA derivatives would signify a useful medium for the advancement of innovative chemical entities to treat infectious diseases, cancer, CNS and cardiovascular system disorders.

REFERENCES

[1] K. Rupinder Gill, K. Ravindra Rawal and J. Bariwal, Recent Advances in the Chemistry and Biology of Benzothiazoles. Arch. Pharm. Chem. Life Sci. 348(2015) 1–24.

[2] M. Henary, S. Paranjpe, E. A. Owens, Substituted benzothiazoles: synthesis and medicinal characteristics. Heterocycl. Comm. 19(2013), 89–99.

[3] P. S. Yadav, D. Devprakash, G. P. Senthilkumar, Benzothiazole different method of synthesis and diverse biological activities. Int. J.Pharm. Sci. Drug Res. ,3(2011)01–07. https://ijpsdr.com/index.php/ijpsdr/article/view/97

[4] X. Xie, Y. Yan, N. Zhu, G. Liu, Highly transparent paper with tunable haze for green electronics.Eur. J. Med. Chem.76(2014), 67–78. DOI: 10.1039/C9RA06368D

[5] Carroll, A.R.; Scheuer, P.J. pentacyclic alkaloids from a tunicate

and its prosobranch mollusk predator Chelynotus semperi. J. Org. Chem. 1990, 55, 4426–4431. [CrossRef]

[6] Gunawardana, G.P.; Kohmoto, S.; Gunasekera, S.P.; McConnel, O.J.; Koehn, F.E. Dercitine, a new biologically active acridine alkaloid from a deep water marine sponge, Dercitus sp. J. Am. Chem. 1988, 110, 4856–4858. [CrossRef]

[7] Noel, S.; Cadet, S.; Gras, E.; Hureau, C. The benzazole scaffold: A SWAT to combat Alzheimer's disease. Chem. Soc. Rev. 2013, 42, 7747–7762. [CrossRef] [PubMed]

[8] Prajapati, N.P.; Vekariya, R.H.; Borad, M.A.; Patel, H.D. Recent advances in the synthesis of 2-substituted benzothiazoles: A review. RSC Adv. 2014, 4, 60176–60208. [CrossRef]

[9] Agarwal, S.; Gandhi, D.; Kalal, P. Benzothiazole: A Versatile and Multitargeted Pharmacophore in the Field of Medicinal Chemistry. Lett. Org. Chem. 2017, 14, 729–742. [CrossRef]

[10] Keri, R.S.; Patil, M.R.; Patil, S.A.; Budagumpi, S. A Comprehensive Review in Current Developments of Benzothiazole-Based Molecules in Medicinal Chemistry. Eur. J. Med. Chem. 2015, 89, 207–251. [CrossRef] [PubMed]

[11] Rouf, A.; Tanyeli, C. Bioactive thiazole and benzothiazole derivatives. Eur. J. Med. Chem. 2015, 97, 911–927. [CrossRef] [PubMed]

[12] Asiri, Y.I.; Alsayari, A.; Muhsinah, A.B.; Mabkhot, Y.N.; Hassan, M.Z. Benzothiazoles as potential antiviral agents. J. Pharm. Pharmacol. 2020, 1459–1480. [CrossRef] [PubMed]

[13] Liu, X.; Dong, Z.-B. A Review on Domino Condensation/Cyclization Reactions for the Synthesis of 2-Substituted 1,3-Benzothiazole Derivatives. Eur. J. Org. Chem. 2020, 4, 408–419. [CrossRef]

[14] M. A. Azam, L. Dharanya, C. C. Mehta, S. Sachdeva, Synthesis and biological evaluation of some novel pyrazolopyrimidines incorporating a benzothiazole ring system. Acta. Pharm. 63(2013), 19–30. DOI: 10.2478/acph-2013-0001

[15] C. Praveen, A. N. Kumar, P. D. Kumar, D. Muralidharan, P. T. Perumal, Camphor sulfonic acid catalyzed a simple, facile, and general method for the synthesis of 2-arylbenzothiazoles, 2-arylbenzimidazoles, and 3H-

spiro[benzo[d]thiazole2,3′-indolin]-2′-ones at room temperature. J. Chem. Sci. 124(2012), 609–624. DOI:10.1007/s12039-012- 0251-3 Hala Shkyair Lihumis et. al./ Prog. Chem. Biochem. Res. 2022, 5(2), 147-164 161

[16] Sadhasivam, G.; Kulanthai, K. Synthesis, characterization, and evaluation of anti-inflammatory and anti-diabetic activity of new benzothiazole derivatives. J. Chem. Pharm. Res. 2015, 7, 425–431.

[17] Tariq, S.; Alam, O.; Amir, M. Synthesis, p38α MAP kinase inhibition, anti-inflammatory activity, and molecular docking studies of 1,2,4-triazole-based benzothiazole-2-amines. Arch. Pharm. Chem. Life Sci. 2018, 351, e1700304. [CrossRef] [PubMed]

[18] Tariq, S.; Kamboj, P.; Alam, O.; Amir, M. 1,2,4-Triazole-based benzothiazole/benzoxazole derivatives: Design, synthesis, p38α MAP kinase inhibition, anti-inflammatory activity and molecular docking studies. Bioorg. Chem. 2018, 81, 630–641. [CrossRef] [PubMed]

[19] Ugwu, D.I.; Okoro, U.C.; Ukoha, P.O.; Gupta, A.; Sunday, N. Novel anti-inflammatory and analgesic agents: Synthesis, molecular docking and in vivo studies. J. Enzyme Inhibit. Med. Chem. 2018, 33, 405–415. [CrossRef]

[20] G. Mariappan, P. Prabhat, L. Sutharson, J. Banerjee, U. Patangia, S. Nath, Synthesis and Antidiabetic Evaluation of Benzothiazole Derivatives. J. Korean Chem. Soc. 56(2012), 251–256. https://doi.org/10.5012/jkcs.2012.56.2.251

[21] J. Cai, M. Sun, X. Wu, J. Chen, P. Wang, X. Zong, M. Ji, Design and synthesis of novel 4-benzothiazole amino quinazolines Dasatinib derivatives as potential anti-tumor agents. Eur. J. Med. Chem. 63(2013), 702– 712. DOI: 10.1016/j.ejmech.2013.03.013

[22] M. M. Choi, E. A. Kim, H. G. Hahn, K. D. Nam, S. J. Yang, S. Y. Choi, T. U. Kim, S. W. Cho, J. W. Huh, Protective effect of benzothiazole derivative KHG21834 on amyloid beta-induced neurotoxicity in PC12 cells and cortical and mesencephalic neurons. Toxicology,239(2007), 156–166. http://www. elsevier.com /locate /ejmech.

[23] Galochkina, A.V.; Bollikanda, R.K.; Zarubaev, V.V.; Tentler, D.G.; Lavrenteva, I.N.; Slita, A.V.; Chirra, N.; Kantevari, S. Synthesis of novel derivatives of 7,8-dihydro-6H-imidazo[2,1-b] [1,3] benzothiazol-5-one and their virus-inhibiting activity against influenza A virus. Arch. Pharm. Chem. Life Sci. 2019, 352, e1800225. [CrossRef] [PubMed]

[24] Montalvão, S.; Leino, T.O.; Kiuru, P.S.; Lillsunde, K.-E.; Yli-Kauhaluoma, J.; Tammela, P. Synthesis and biological evaluation of 2-amino-benzothiazole and benzimidazole analogs based on the clathrodin structure. Arch. Pharm. Chem. Life Sci. 2016, 349, 137–149. [CrossRef]

[25] Takamatsu, Y.; Aoki, M.; Bulut, H.; Das, D.; Amano, M.; Sheri, V.R.; Kovari, L.C.; Hayashi, H.; Delino, N.S.; Ghosh, A.K.; *et al*. Novel Protease Inhibitors Containing C-5-Modified bis-Tetrahydrofuranylurethane and Aminobenzothiazole as P2 and P20 Ligands That Exert Potent Antiviral Activity against Highly Multidrug-Resistant HIV-1 with a High Genetic Barrier against the Emergence of Drug Resistance. Antimicrob. Agents Chemother. 2019, 63, e00372. [CrossRef]

[26] Wu, H.; Bock, S.; Snitko, M.; Berger, T.; Weidner, T.; Holloway, S.; Kanitz, M.; Diederich, W.E.; Steuber, H.; Walter, C.; *et al*. Novel Dengue Virus NS2B/NS3 Protease Inhibitors. J. Antimicrob. Agent. Chemother. 2015, 59, 1100–1109. [CrossRef]

[27] Ghosh, A.K.; Nyalapatla, P.R.; Kovela, S.; Rao, K.V.; Brindisi, M.; Osswald, H.L.; Amano, M.; Aoki, M.; Agniswamy, J.; Wang, Y.-F.; *et al*. Design and Synthesis of Highly Potent HIV-1 Protease Inhibitors Containing Tricyclic Fused Ring Systems as Novel P2 Ligands: Structure–Activity Studies, Biological and X-ray Structural Analysis. J. Med. Chem. 2018, 61, 4561–4577. [CrossRef]

[28] Ghosh, A.K.; Rao, K.V.; Nyalapatla, P.R.; Osswald, H.L.; Martyr, C.D.; Aoki, M.; Hayashi, H.; Agniswamy, J.; Wang, Y.-F.; Bulut, H.; *et al*. Design and Development of Highly Potent HIV-1 Protease Inhibitors with a Crown-Like Oxotricyclic Core as the P2-Ligand to Combat Multidrug-Resistant HIV Variants. J. Med. Chem. 2017, 60, 4267–4278. [CrossRef]

[29] Elamin, M.B.; Elaziz, A.A.E.S.A.; Abdallah, E.M. Benzothiazole moieties and their derivatives as antimicrobial and antiviral agents: A mini-review. Int. J. Res. Pharm. Sci. 2020, 11, 3309–3315. [CrossRef]

[30] Probst, P.; Grigg, J.B.; Wang, M.; Muñoz, E.; Loo, Y.-M.; Ireton, R.C.; Gale, M., Jr.; Iadonato, S.P.; Bedard, K.M. A small-molecule IRF3 agonist functions as an influenza vaccine adjuvant by modulating the antiviral immune response. Vaccine 2017, 35, 1964–1971. [CrossRef] [PubMed]

[31] Shaikh, F.M.; Patel, N.B.; Sanna, G.; Busonera, B.; Colla, P.L.; Rajani, D.P. Synthesis of some new 2-amino-6-thiocyanato benzothiazole derivatives bearing 2,4-thiazolidinediones and screening of their in vitro antimicrobial, antitubercular and antiviral activities. Med. Chem. Res. 2015, 24, 3129–3142. [CrossRef]

[32] A.C. Razus, L. Birzan, N.M. Surugiu, A.C. Corbu, F. Chiraleu, Syntheses of azulen-1-yl-benzothiazol-2-yl aiazenes, Dyes Pigments 74 (2007) 26-33.

[33] T. Reemtsma, O. Fiehn, G. Kalnowski, M. Jekel, Microbial transformations and biological effects of fungicide-derived benzothiazoles determined in industrial waste water, Environ. Sci. Technol. 29 (1995) 478e485.

[34] R.L. Parton, D.A. Stegman, K.W. Williams, V. L. Chand, Benzothiazole, benzoselenazole or benzooxazole sensitizers for photographic films, 1995,61-81, US5516628 A.

[35] A. Rana, N. Siddiqui, S.A. Khan, S. Ehtaishamul Haque, M.A. Bhat, N-{[(6-substituted-1,3-benzothiazole-2-l) amino]carbonothioyl}-2/4-substituted benzamides: synthesis and pharmacological evaluation, Eur. J. Med. Chem. 43 (2008) 1114-1122.

[36] C. Gan, L. Zhou, Z. Zhao, H. Wang, Benzothiazole Schiff-bases as potential imaging agents for b-amyloid plaques in Alzheimer's disease, Med. Chem. Res. 22 (2013) 4069-4074.

[37] Livio Racane, Vesna Tralic-Kulenovic, David W. Boykin and Grace Karminski-Zamola, Synthesis of New Cyano-Substituted bis-Benzothiazolyl Arylfurans and Arylthiophenes. Molecules,8(2003) (3) 342-348; https://doi.org/10.3390/80300342

[38] G.P. Gunawardana, S. Kohmoto, S.P. Gunesakara, O.J. McConnel, F.E. Koehn, Dercitine, a new biologically active acridine alkaloid from a deep water marine sponge, Dercitus sp, J. Am. Chem. Soc. 110 (1988) 4856-4858.

[39] Z. Cao, F. Qiu, Q. Wang, G. Cao, L. Zhuang, Q. Shen, X. Xu, J. Wang, Q. Chen, D. Yang, Synthesis of azo benzothiazole polymer and its application of 1-2 Y-branched and 2-MacheZehnder interferometer switch, Optik-Int J. Light Elec. Opt. 124 (2013) 4036-4040.

[40] Sumit, Arvind Kumar, Arun Kumar Mishra, Advancement in Pharmacological Activities of Benzothiazole and its Derivatives: An Up to Date Review, Mini Rev Med Chem, 2021; 21(3): 314-335. doi: 10.2174/1389557520666200820133252.

[41] S. Rangappa Keri, Mahadeo Patil, A comprehensive review in current developments of benzothiazolebased molecules in medicinal chemistry. European Journal of Medicinal Chemistry 89(2015)207-251, DOI:10.1016/j.ejmech.2014.10.059.

[42] K.W. Seo, M. Park, J.G. Kim, T.W. Kim, H.J. Kim, Effects of benzothiazole on the xenobiotic metabolizing enzymes and metabolism of acetaminophen, J. Appl. Toxicol. 20 (2000) 427-430

[43] T. Reemtsma, Determination of 2-substituted benzothiazoles of industrial use from water by liquid chromatography/electrospray ionization tandem mass spectrometry, Rapid Commun. Mass Spectrom. 14 (2000) 1612e1618

[44] Shaista Amin, Amrita Parle. BENZOTHIAZOLE - A MAGIC MOLECULE. I nternational Journal of Pharmaceutical Sciences and Research; Vol. 8(12): 4909-4929.

[45] Shaista Amin, Amrita Parle. Benzothiazole - A Magic Molecule. I nternational Journal of Pharmaceutical Sciences and Research; Vol. 8(12): 4909-4929.

[46] Lihumis H.S., Alameri A. A., Zaooli Rawaa Hefdhi. A Review on Recent Development and biological applications of benzothiazole derivatives. Progress in Chemical and Biochemical Research, 2022, 5(2), 147-164.

[47] Bele, D.S., Kothari, H., and Singhvi, I. Synthesis and

antimicrobial activity of some benzothiazole derivatives. Inter. J. Pharm. and Chem. Sci., 1(2012) (4)1238-1242.

[48] T. Nogrady, F. D. Weaver, Medicinal Chemistry: AMolecular and Biochemical Approach, Oxford University Press, New York (2005)559.

[49] Shinde PK and Waghamode KT: Synthesis, characterization and antibacterial activity of substituted benzothiazole derivatives. International Journal of Scientific and Research Publications. 7(2017) (8)365-370.

[50] Maddila S, Gorle S, Seshadri N, Lavanya P and Jonnalagadda SB: Synthesis, antibacterial and antifungal activity of novel benzothiazole pyrimidine derivatives. Arabian Journal of Chemistry .9(2016) (5) 681-687.

[51] M. Singh, M. Gangwar, G. Nath, S. K. Singh, DNA cleavage and antimicrobial activity of 4-thiazolidinones-benzothiazole conjugates. Indian J.Exp. Biol. 52(2014)1062–1070.

[52] D. S. Bele, H. Kothari and I. Singhvi: Synthesis and antimicrobial activity of some benzothiazole derivatives. International Journal of Pharmaceutical and Chemical Sciences 1(2012) (4) 1238-1242.

[53] P. K. Sahu, S. K. Gupta, D. Thavaselvamd, D. D. Agarwal, Synthesis and evaluation of antimicrobial activity of 4H-pyrimido[2,1-b]benzothiazole, pyrazole and benzylidene derivatives of curcumin . Eur. J. Med. Chem. 54(2012), 366–378.

[54] I. H. R. Tomi, J. H. Tomma, A. H. R. Al-Daraji, A. H. Al-Dujaili, J. Saudi Chem. Soc. 2012, Synthesis, characterization and comparative study the microbial activity of some heterocyclic compounds containing oxazole and benzothiazole moieties IHR Tomi, JH Tomma, AHR Al-Daraji, AH Al-Dujaili. Journal of Saudi Chemical Society 19(2015) (4)392-398

[55] B.Gurupadyya , M.Gopal , B.Padmashali and Y.Manohara : Synthesis and pharmacological evaluation of azatidin-2-ones and thiazolidine-4-ones encompassing benzothiazole. Indian J Pharm Sci. 70(2008) (5) 572-577.

[56] F.Mir , S.Shafi , M.S.Zaman ,N.P. Kalia , V.S.Rajput , C.Mulakayala , N.Mulakayala , I.A.Khan and M.S.Alam : Sulfur rich 2-mercaptobenzothiazole and 1,2,3-

triazole conjugates as novel antitubercular agents. European Journal of Medicinal Chemistry. 76(2014) 274-243.

[57] A.K. Verma, A. Martin and A.K. Singh: Synthesis, Characterization and evaluation of Anti-inflammatory and Analgesic activity of Benzothiazole derivatives. Indian Journal of Pharmaceutical and Biological Research (IJPBR). 2(2014) (3): 84-89

[58] V. N. Telvekar, V. K. Bairwa, K. Satardekar, A. Bellubi, Novel 2-(2-(4-aryloxybenzylidene) hydrazinyl)benzothiazole derivatives as antitubercular agents. Bioorg. Med. Chem. Lett. 22(2012) 649–652.

[59] Z. Wang, X. Shi, J. Wang *et al*., "Synthesis, structure activity relationships and preliminary antitumor evaluation of benzothiazole-2-thiol derivatives as novel apoptosis inducers," Bioorganic and Medicinal Chemistry Letters, vol. 21, no. 4, pp.1097–1101, 2011.

[60] Lindgren EB, De Brito MA, Thatyana RA, Vasconcelos, de Moraes MO, Montenegro RC, Yoneda JD and Leal KAZ: Synthesis and anticancer activity of (E)-2-benzothiazole hydrazones. European Journal of Medicinal Chemistry 2016; 86: 12-16.

[61] S. Amin and A. Parle: Synthesis, characterization and antioxidant activity of 2-aryl benzothiazole derivatives. International Journal of Current Pharmaceutical Research. 10 (2018) (5) 3-8. DOI:10.22159/ijcpr.2018v10i5.29685

[62] O. Guzel, N. Karali, N.Ozsoy, S. Ozbey and A. Slman : Synthesis of new spiroindolinones incorporating a benzothiazole moiety as antioxidant agents. European Journal of Med Chem 45(2010) 1068-1077.

[63] D. Cressier, C. Prouillac, P. Hernandez, C. Amourette, M. Diserbo, C. Lion and G. Rima: Synthesis, antioxidant properties and radioprotective effects of new benzothiazoles and thiadiazoles. Bioorganic and Medicinal Chemistry 17(2009): 5275-5284

[64] Cabrera-Perez LC, Padilla-Martınez II, Cruz A, Mendieta - Wejebe JE, Tamay-Cach F and RosalesHernandez MC: Evaluation of a new benzothiazole derivativewith antioxidant activity in the initial phase of acetaminophen toxicity. Arabian

Journal of Chemistry 12(2016) 8: 1-12. https://orcid.org/0000- 0002-6064-1040

[65] E. Meltzer-Mats, G. Babai-Shani, L. Pasternak, N. Uritsky, T. Getter, O. Viskind, J. Eckel, E. Cerasi, H. Senderowitz, S. Sasson and A. Gruzman: Synthesis and mechanism of hypoglycemic activity of benzothiazole derivatives. Journal of Medicinal Chemistry 56(2013) (13) 5335-5350. https://doi.org/10.1021/jm4001488

[66] G. Mariappan, P. Prabhat, L. Sutharson, J. Banerjee, U. Patangia and S. Nath: Synthesis and antidiabetic evaluation of benzothiazole derivatives. Journal of the Korean Chemical Society. 56 (2012) (2) 251-256. https://doi.org/10.5012/jkcs.2012.56.2.251.