

BENZOTHAZOLES: A REVIEW OF THEIR PHARMACOLOGICAL EFFECTS AND THERAPEUTIC POTENTIAL

R. Padma ¹, M. Yagna Sri ², D. Swathi ³, M. Ajay babu ⁴, R. Amareswari ⁵, Sk. Abdul Gafoor ⁶.

¹ Department of pharmaceutical chemistry, A.M Reddy memorial college of pharmacy, Petlurivaripalem, Narasaraopet, Palnadu-522601, Andhra Pradesh, India.

^{2,3,4,5,6} B. Pharmacy Students A.M Reddy memorial college of pharmacy, Petlurivaripalem, Narasaraopet, Palnadu-522601, Andhra Pradesh, India.

ABSTRACT

Benzothiazoles are a class of heterocyclic compounds that have garnered significant attention in recent years due to their diverse biological activities. This review aims to provide a comprehensive overview of the pharmacological effects and therapeutic potential of benzothiazoles. The compounds have been found to exhibit anticancer, antidiabetic, anti-inflammatory, antibacterial, antifungal and antimalarial properties, making them potential candidates for the treatment of various diseases. The unique structure of benzothiazoles allows for the development of novel drugs with improved efficacy and safety profiles. This review highlights the current state of knowledge on benzothiazoles and their potential application in medicine, emphasizing their therapeutic potential and encouraging future research into these versatile compounds.

KEYWORDS: Benzothiazoles, Heterocyclic compounds, Pharmacological effects, Therapeutic potential.

INTRODUCTION

Heterocyclic compounds are those cyclic compounds whose rings contain one or more atoms of other elements besides carbon. The non carbon atoms such as rings, are refer to as hetero atoms. The most common hetero atoms are nitrogen, sulphur and oxygen. The wide distribution of heterocyclic compounds in nature makes them particularly important due to their extensive range of physiological activities [1]. Benzothiazoles are one of the hetero cyclic compounds. Organic chemistry and drug discovery hold great significance for benzothiazoles because of their diverse range of physiological functions [2]. Benzothiazoles and its derivatives have been found to exhibit a wide range of pharmacological action [3,4]. The promise of benzothiazoles derivatives lies in their unique structures and broad range of biological effects. Benzothiazole derivatives have gained attention because of their diverse biological properties such as Anticancer, Analgesic, Anti Inflammatory, Anti Diabetic, Fungicidal activity, Anti Malaria, etc. And currently benzothiazole moieties are thought to be diagnostic agents for budding amyloid binding in neuro degenerative disease, selective fatty acid amide hydrolase inhibitors, etc. [5]. Benzothiazole derivatives come across for chemical research as in polymer chemistry, dyes, drugs, etc. Benzothiazole compounds and their derivatives are still being researched for their potential applications and properties [6].

LITERATURE REVIEW

ANTICANCER ACTIVITY

Ali Irfan et. al., who had reported that benzothiazole derivatives as anticancer agents. Benzothiazole derivatives like benzothiazole aniline belongs to the hetero cyclic class of bicyclic compounds. Benzothiazole aniline

derivatives possess broad spectrum biological activities such as anticancer, antitumour, antiviral, antidiabetic, etc. the benzothiazoles scaffolds has a significant effect on the inhibition of the metal enzyme carbonic anhydrous. Over the last decade, an extensive literature survey has revealed that benzothiazole derivatives are primarily used as anticancer agents. The effectiveness of these compounds against various cancer cell lines is achieved through a variety of mechanism some of which are poorly studied or comprehended. The inhibition of tumours associated caused by benzothiazole aniline derivatives is on the other hand better investigated and such compounds may serve as anticancer leads for the developments of agents effective against hypoxic tumours agent.[7],[8]

ANTIDIABETIC ACTIVITY

Khyati-Bhagdev.et.al., Who had reported that benzothiazole as an antidiabetic agent. Diabetes is a disease that progresses slowly and effects the major organs of the human body including the heart, kidney, blood vessels, liver and kidneys. Numerous hypoglycaemic drugs are available on the market. Benzothiazole derivatives are excellent hypoglycaemic agents. Hypoglycaemic agents can also be beneficial through the use of benzothiazole derivatives. Researchers are constantly working on the benzothiazole molecules to develop more potent derivatives that can be utilized as antidiabetic drugs. We hope this review article will provide all the information about benzothiazole moieties as antidiabetic agents like structure activity relationship of benzothiazole derivatives as antidiabetic agents, synthesis schemes for the derivation of novel antidiabetic benzothiazole derivatives and invitro and in vivo methods for the evaluation of hypoglycaemic agents of novel synthesized compounds.[9],[10]

ANTIHELMINTIC ACTIVITY

G aware Vinayak. M. et. al., who had reported that synthesis and evaluation of benzothiazole derivatives for anthelmintic activity. Synthesis and evaluation of benzothiazole derivatives revealed their anthelmintic activity. 2-amino benzo thiazole was converted to 6-substituted derivatives of 2-amino benzothiazoles by nitration and bromination. Reaction to yield 6-nitro 2-amino benzothiazole respectively. The derivative which included 2-amino benzothiazole were further processed with chloro acetyl chloride to produce chloro acetamido derivative of benzothiazole. More over the product is subjected to various heterocyclic and aromatic amines conformation of the synthesized compound was provided by IR, 1-HNMR and mass spectral data. The study focused on the anthelmintic activity of synthetic substituted benzothiazole derivatives against Indian adult earth worms at various concentration. It was observed that the new synthesized compounds possessing electron withdrawing group at 6th position of benzothiazole nucleus and substituted chloro-fluor 3rd position of aromatic amine exhibited higher anthelmintic activity compared to that of other synthesized compounds. The current research is focussed on the various synthesis method for substituted benzothiazoles with potential anthelmintic activity that are currently being developed.

ANTIBACTERIAL ACTIVITY

Marina Gjorgjieva, et. al., who had reported that benzothiazole based compounds in anti-bacterial drug discovery. The literature has reported numerous compounds with a benzothiazole scaffold that exhibit promising activity against various gram positive and negative bacteria's as well as mycobacterium tuberculosis. Benzothiazole based anti-bacterial compound bind to different biological targets in bacterial cell and have been shown to be inhibitors of enzymes that are important for essential processes in bacterial cell such as cell wall synthesis, cell division, and DNA replication are important for different biosynthesis pathways of essential compound in bacterial cells such as the biosynthesis of the histidine and biotin. The purpose of this review is to explore the anti-bacterial potential of benzothiazole based compounds specifically their interaction with bacterial cells. We assess the importance of benzothiazole scaffolds in the discovery of new anti-bacterial compounds against resistant bacterial strains, optimization of their anti-bacterial activity and the future prospective of benzothiazole based anti-bacterial.[11],[12]

ANTIVIRAL ACTIVITY

Yahya Asiri, et. al., who had reported that benzothiazoles as potential antiviral agents. Benzothiazole plays a pivotal role in the design and development of anti-viral drugs. This is evident from the fact that it comprises many clinically useful agents. The current review is designed to offer an overview of the recent development of benzothiazole based anti-viral agents, with an emphasis on their structure activity relationships and lead optimization. This review highlights 64 potential novel lead molecule and main findings, which were identified from a total of 105 articles. We are optimistic that this review will provide a rational approach to the significance

of improving the future designing of novel broad spectrum benzothiazole based anti-viral agent that can be used to fight emerging viral diseases.[13]

ANTIOXIDANT ACTIVITY

Amritha Parle, et. al., who had reported that synthesis, characterization and anti-oxidant activity of novel 2-aryl benzothiazole derivatives were synthesized reaction were monitored using TLC technique and the newly synthesized derivative were characterized by ATIR and proton nuclear magnetic resonance technique. Anti-oxidant assay was performed using 2,2 amino -bis [3 methyl benzothiazoline, 6-sulfonic acid] [ABTS] method and 2,2 diphenyl -1-picryl hydrazyl [DPPH] method. The anti-oxidant activity was found to be better in ABTS assay then compared to DPPH assay. It was found that the synthesized benzothiazole derivative showed significant radicle scavenging potential.[14],[15].

ANTIMARIAL ACTIVITY

Linh Tran, et. al., who had reported that antimalarial activities of benzothiazole analogous. There's evidence that benzothiazole derivatives have a wide range of biological activities, which include antimalarial activity. The purpose of this systematic review is to summarize and evaluate the antimalarial effect of benzothiazole analogous. In October 2017 we conducted an electronic search using nine data base and then updated it in September 2022. We included all original in vivo 4studies that documented the antimalarial activities of compounds containing benzothiazole analogous with no restriction. The risk of bias of each included study was assessed by ToxRTool. Our study included 28 articles that were either invitro and in vivo or both. There were 232 substances that were found to have potent anti plasmodial activity against different strains of the malaria parasite. Different antimalarial mechanisms are present in benzothiazole analogous, such as inhibition of plasmodium falciparum enzymes in invitro and blood parasites inhibition in in vivo experiments. Their sale revenue as grew significantly. It's not what I anticipated. Benzothiazole derivatives are promising substances for treating malaria. The structure- activity relationship studies suggest that the substitution pattern of the benzothiazole scaffolds plays a crucial role in determining the antimalarial activity of the analogous.[16],[17]

ANTIFUNGAL ACTIVITY

Dhamak kiran Bhausheb.et. al., who Had Reported that synthesis And Evaluation of Antifungal activity Of Benzothiazole derivatives. Derivatives of Benzothiazoles were synthesized and evaluated for their antifungal activity.2-amino benzothiazole was first converted to 6 substituted derivatives of 2-amino benzothiazole by nitration and bromination reaction to yield 6-nitro-2-amino benzothiazole and 6-bromo-2-amino benzothiazole respectively. All the derivatives including 2-amino benzothiazole were further treated with chloro acetyl chloride to form chloro acetamido derivatives of benzothiazole. Further the product is treated with various hetero cyclic and aromatic amines. The synthesized compound was confirmed by IR, ¹HNMR and Mass spectral data. Synthesized substituted benzothiazole derivatives were investigated for their antifungal activity which was evaluated by the tube dilution method [turbidimetric method]. It was observed that the new synthesized compounds possessing electron with drawing 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.[18]

REFERENCES

1. Gupta R. R., Kumar M., and Gupta V., published by Springer in 1998, is **10.1007/978-3- 64272276-9**
2. Ingle RG, Marathe RP Review on literature study of benzothiazole. Int J Pharmaceutical Research allied sci.2012;1[4]:11-15.
3. Khare E, S. Sharma, Singh Y Keshri.P. A comprehensive review on the biological aspects of emerging benzothiazole. Pharma. 2019;20[1];1-8.
4. Pathak N, Rathi E, Kumar N, Kini SG, Rao, CM, A review on anti-cancer potentials of benzothiazoles. Mini-Rev Med Chem. 2020; 20[1];12-23.
5. Gan C, Zhou L, Zhao Z, wang H, Benzothiazole Schiff-bases as Potential imaging agents for b-amyloid plaques in Alzheimer's disease. Med Chem Res.2013;22[9]:4069-74. doi:10.1007/s00044-012-0416-0.

6. Asif M, Imran M. A mini-review on pharmacological importance of benzothiazole scaffold. *Rev organic Chem.*2021;18[8]:1086-1097.
7. Akhtar J, Khan AA, Ail Z. SAR relationship study and design strategies of nitrogen containing heterocyclic moieties for their anticancer activities. *Eur J Med chem* 2017; 5:143-89-PubMeb.
8. Keri SR, Patil RM, Patil AS, Budagumpi S.A comprehensive review in current developments of benzothiazole- based molecules in medicinal chemistry. *Eur J Med Chem* 2015; 89:207-51.
9. Tirupathi KD. *Essentials of medical pharmacology.* JP Medical Ltd; 2013 september 30.
10. Rang HP, Dale MM. *Rang and Dale's pharmacology.* Elsevier Brasil; 2007.
11. Cantas, L.; Shal, S. Q. A.; Cavaco, L.M.; Manaia, C.M.; Walsh, F.; Popowska, M.; Garelick, H.; Burgmann, H.; Sorum, H.A brief multi-disciplinary review on antimicrobial resistance in medicine and its linkage to the global environmental microbiota, *Front. Microbial.*, 2013,14,4,96.
12. Livermore, D., M. Has, Has the era of untreatable infections arrived? *J. Anti microb. Chemother.*, 2009 64, i29-i36.
13. Cavicchioli R et al. Scientists' warning to humanity; microorganisms and climate change. *Nat Rev Microbial* 2019; 17: 569-586.
14. B. Poljsak, D. Suput, I. Milisav, *Oxidative Medicine and Cellular Longevity.*, 2013, 11.
15. M. MOEIN, S. MOEIN, S. Ahmadizadeh, *Molecules.*, 2008, 13, 2804-2813.
16. Snow RW, Guerra CA, Noor AM, Myint HY, Hay SI. The global distribution of clinical episodes of *Plasmodium falciparum* malaria. *Nature.* 2005; 434[7030]:214-217
doi:10.1038/nature03342.
17. Greenwood B, Salisbury D, Hill AV. Vaccines and global health. *Philos Trans R Soc Lond B Biol Sci.* 2011; 366[1579]: 2733-2742.
doi: 10.1098/rstb.2011.0076.
18. Masao, Y., Ichiro, H., Noriyuki, H., Toshinori, A., Youko, O., and Fumie, T., 2005, synthesis and biological evaluation of benzothiazole derivatives as potent antitumour agents, *Bioorg Med Chem Lett.*, 15, pp. 332-82.