



International Journal of Innovative Research in Science Engineering and Technology (IJIRSET)

(A Monthly, Peer Reviewed, Refereed, Scholarly Indexed, Open Access Journal)



Impact Factor: 8.524

Volume 14, Issue 1, January 2025

In Vivo Evaluation of Benzothiazole Derivatives for Anti-Tumor and Anti-Malarial Activities: A Comprehensive Study

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ABSTRACT: Benzothiazole derivatives have garnered significant attention in drug discovery due to their diverse pharmacological properties. This study investigates the in vivo anti-tumor and anti-malarial activities of novel benzothiazole derivatives, aiming to evaluate their therapeutic potential.

KEYWORDS: Benzothiazole, in vivo, anti-tumor and anti-malarial.

I. INTRODUCTION

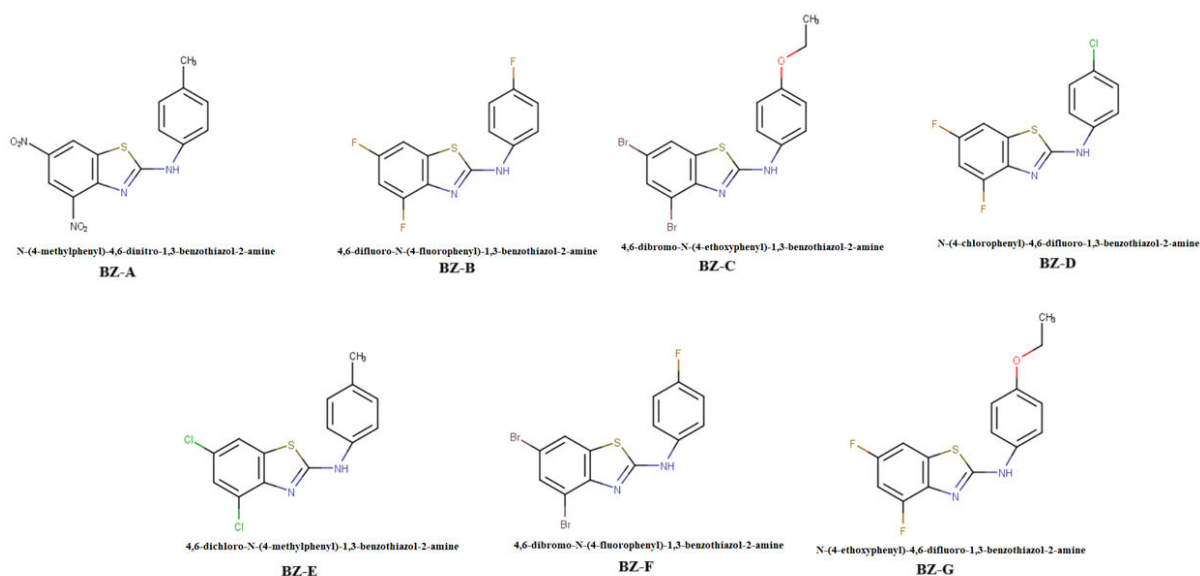
Cancer is a complex and multifaceted disease characterized by the uncontrolled growth and spread of abnormal cells. It remains a significant global health challenge due to its high morbidity and mortality rates, as well as its diverse manifestations across different tissues and organ systems. Cancer continues to pose significant obstacles for the development of safer, more effective treatments and cures. Similarly, malaria remains a widespread and fatal disease, affecting nearly 40% of the global population, particularly in developing countries, according to the WHO. The prevalence of malaria has made it a serious public health threat, and its control is now a global priority. *Plasmodium falciparum*, the most dangerous species of the parasite, causes the most severe form of malaria in humans. The increasing emergence of drug-resistant strains has compromised the effectiveness of current treatments, creating an urgent need for new therapies.

Developing a new generation of antimalarial drugs is critical, particularly those targeting essential biological pathways for parasite survival and disease progression. Heterocyclic compounds like benzothiazole play an important role due to their versatile biological activities. Benzothiazole and its derivatives have been extensively researched for their potential to treat a variety of diseases. The synthesis of these derivatives remains a key focus in research, with new synthetic techniques and modifications enhancing their biological properties and specificity. This ongoing investigation into the pharmacological potential of benzothiazole derivatives holds promise for the development of innovative treatments.

II. RESEARCH METHODOLOGY

Benzothiazole derivatives: Four benzothiazole derivatives (A, B, C and D) were studied for their anti-tumor activity and three benzothiazole derivatives (E, F and G) for antimalarial activity.

Fig 1: Novel Benzothiazole Compounds



In Vivo anti-tumor activity: Female Swiss albino mice, weighing between 25 and 30 grams, were used to assess the antitumor activity of synthesized compounds after being inoculated with Ehrlich ascites carcinoma (EAC). The EAC cells were obtained for the study, and the anticancer effectiveness of the compounds was evaluated. The mice were divided into groups according to the compounds administered. On day zero, the mice were weighed and given an intraperitoneal injection of 2.5×10^6 EAC cells per mouse. After 3 days, the animals began receiving doses of the test compounds. On day 18, the mice were weighed again, and the mean survival time (MST) was recorded for each group. The effect of the compounds on the percentage changes in body weight is also presented.

In Vivo Antimalarial Activity: The in vivo antimalarial activity was assessed using a modified version of the Peters 4-day suppressive test. In brief, 0.2 ml of an infected blood suspension containing 1×10^5 P. berghei NK65 pRBCs was administered intraperitoneally to mice. The animals were randomly assigned to groups of five. Mice in the test groups were treated subcutaneously with compounds at a dose of 200 mg/kg/day. The negative control group (Normal) received 0.2 ml of the vehicle (2% DMSO in water). Treatment began 24 hours after the inoculation with P. berghei and continued for 4 days. Mortality was monitored daily across all groups for 40 days following the inoculation.

III. OBSERVATION

In Vivo Anti-tumor Activity: BZ-A caused a 15.6% increase in body weight and had an MST of 31 days, indicating limited effectiveness and significant tumor progression. BZ-B, with a 68.5% increase in body weight and an MST of 52 days, exhibited the highest anti-tumor activity, closely approximating the normal group and suggesting its strong therapeutic potential. BZ-C led to a 17.4% increase in body weight and an MST of 26 days, reflecting significant tumor growth and reduced survival time, which is unfavorable compared to the normal group. BZ-D resulted in a 7.7% increase in body weight and an MST of 47 days, demonstrating moderate anti-tumor activity, though slightly less effective than BZ-B. The normal group showed a 7.5% increase in body weight and an MST of 55 days, serving as a reference for untreated animals. Overall, the MSTs and body weight changes of BZ-A, BZ-B, BZ-C, and BZ-D indicate varying levels of anti-tumor effectiveness. BZ-B and BZ-D demonstrated relatively better outcomes, with BZ-B emerging as the most promising candidate for further development. In contrast, BZ-A and BZ-C displayed limited efficacy, suggesting the need for structural modifications or dosage optimization to enhance their anti-tumor potential.

Table 1: Observed Anti-tumor Activity

Compound Administered	Change in body weight (%)	MST (Mean Survival Time) (days)
Normal Group	7.5	55
BZ-A	15.6	31
BZ-B	68.5	52
BZ-C	17.4	26
BZ-D	7.7	47

Fig 2: Observed Anti-tumor Activity (Change in body weight)

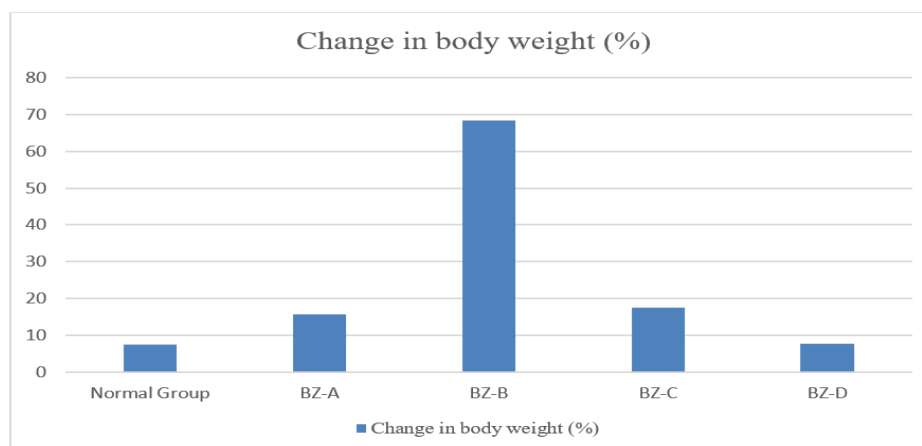
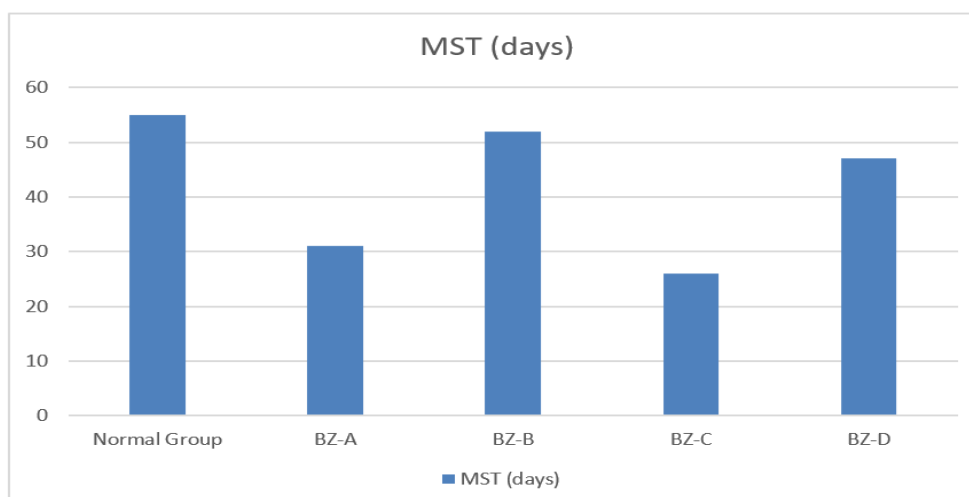


Fig 3: Observed Anti-cancer Activity (MST)



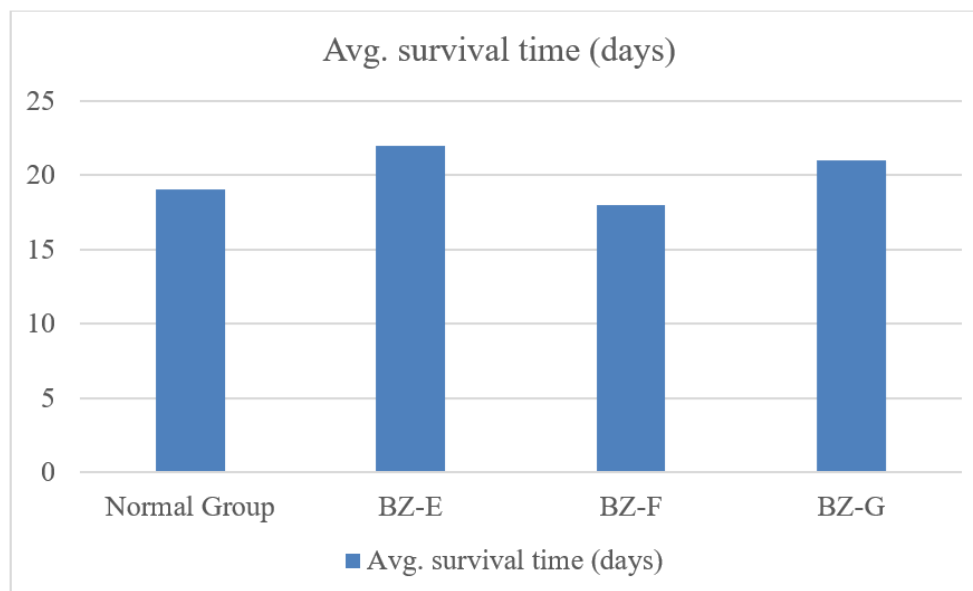
The SAR analysis of compounds BZ-A, BZ-B, BZ-C, and BZ-D reveals distinct variations in anti-tumor activity based on their structural differences. BZ-A, with a 4-methylphenyl group and 4,6-dinitro substituents, exhibited poor activity (15.6% body weight increase, MST: 31 days), likely due to steric hindrance and limited interactions with the target. BZ-B, featuring a 4-fluorophenyl group and 4,6-difluoro substituents, displayed the best anti-tumor activity (68.5% body weight increase, MST: 52 days), attributed to the electron-withdrawing fluoro group enhancing binding affinity. BZ-C, bearing a 4-ethoxyphenyl group and 4,6-dibromo substituents, showed poor activity (17.4% body weight increase, MST: 26 days), possibly due to bulky groups reducing target interaction. BZ-D, with a 4-chlorophenyl group and 4,6-difluoro substituents, demonstrated moderate activity (7.7% body weight increase, MST: 47 days), as the smaller chloro group provided better binding than the bulkier ethoxy group in BZ-C. Overall, the SAR highlights that smaller and electron-withdrawing substituents (BZ-B and BZ-D) enhance activity, while bulkier groups (BZ-A and BZ-C) reduce effectiveness.

In Vivo Antimalarial Activity: The study evaluates the anti-malarial activity of benzothiazole derivatives (BZ-E, BZ-F, and BZ-G) by analyzing their average survival time (AST) in comparison to the normal group. The results provide insights into the effectiveness of these compounds in extending survival time in the context of *Plasmodium berghei* infection. The normal group exhibited an average survival time of 19 days, representing the baseline survival for untreated subjects. Among the tested compounds, BZ-E showed the longest survival time (22 days), indicating notable anti-malarial activity and suggesting its potential effectiveness and enhancing host survival. BZ-G demonstrated a slightly shorter survival time (21 days), which still represents an improvement over the normal group, highlighting its moderate anti-malarial potential. In contrast, BZ-F showed an AST of 18 days, which was slightly lower than the normal group, suggesting limited or negligible anti-malarial activity at the tested dosage. Overall, the results indicate that BZ-E and BZ-G exhibit promising anti-malarial activity, with BZ-E emerging as the most effective candidate for further investigation. BZ-F, however, appears to have minimal impact on survival time, requiring optimization in structure or dosage to enhance its efficacy.

Table 2: Observed Antimalarial Activity

Compound Administered	Avg. survival time (days)
Normal Group	19
BZ-E	22
BZ-F	18
BZ-G	21

Fig 4: Observed Antimalarial Activity



The SAR study of benzothiazole derivatives (BZ-E, BZ-F and BZ-G) against *Plasmodium berghei* reveals the following: BZ-E, containing a 4-methylphenyl group with 4,6-dichloro substituents, demonstrated the highest anti-malarial activity with an AST of 22 days, likely due to the smaller, electron-withdrawing chloro groups enhancing binding and parasitemia suppression. BZ-G, with a 4-ethoxyphenyl group and 4,6-difluoro substituents, showed moderate activity (AST: 21 days), as the ethoxy group's bulk may reduce binding efficiency compared to the smaller methyl group in BZ-E. BZ-F, featuring a 4-fluorophenyl group and 4,6-dibromo substituents, had the lowest activity (AST: 18 days, below the normal group), possibly due to steric hindrance from the bulky bromo groups interfering with target interactions. In summary, smaller substituents (BZ-E and BZ-G) improved anti-malarial activity, with BZ-E being the most effective. Structural modifications, especially for BZ-F, are necessary to enhance efficacy.

IV. CONCLUSION

The comprehensive in vivo evaluation of benzothiazole derivatives in this study underscores their potential as agents for combating cancer and malaria. The results demonstrate that these derivatives exhibit significant antitumor and antimalarial activities, highlighting their ability to inhibit tumor cell proliferation and induce apoptosis, as well as effectively suppress the growth of *Plasmodium*. The structural modifications of benzothiazole compounds enhanced their pharmacological profiles, improving their bioavailability and potency. While the findings are promising, further research is required to fully understand the mechanisms of action, optimize dosages, and assess long-term safety and efficacy.

REFERENCES

1. Elrazig, Amani & Izzeldin, Ishraga & Abdallah, Emad & Eltieb, Nawadir. (2020). Evaluation of some new synthesis benzothiazole and benzimidazole Derivatives as potential antimicrobial and anticancer agents. *International Journal of ADVANCED AND APPLIED SCIENCES*. 7. 69-77. 10.21833/ijaas.2020.02.010.
2. Hadanu, Ruslin & Adelin, La & Sutapa, I Wayan. (2018). QSAR Studies of Nitrobenzothiazole Derivatives as Antimalarial Agents. *Makara Journal of Science*. 22. 10.7454/mss.v22i1.7620.
3. Hadanu, Ruslin & Idris, Salim & Sutapa, I Wayan. (2015). QSAR Analysis of Benzothiazole Derivatives of Antimalarial Compounds Based On AM1 Semi-Empirical Method. *Indonesian Journal of Chemistry*. 15. 86-92. 10.22146/ijc.21228.
4. Hout, S & Azas, Nadine & Darque, A & Robin, Maxime & Giorgio, C & Gasquet, M & Galy, J. & Timon-David, P. (2004). Activity of benzothiazoles and chemical derivatives on *Plasmodium falciparum*. *Parasitology*. 129. 525-35. 10.1017/S0031182004006031.

5. Irfan, Ali & Batool, Fozia & Naqvi, Syeda Andleeb & Islam, Amjad & Osman, Sameh & Nocentini, Alessio & Alissa, Siham & Supuran, Claudiu. (2019). Benzothiazole derivatives as anticancer agents. *Journal of Enzyme Inhibition and Medicinal Chemistry*. 35. 265-279. 10.1080/14756366.2019.1698036.
6. Kumar, Gaurav & Singh, Sanjay & Negi, Manisha & Abhishek, (2024). An In-Depth Analysis of Benzothiazole Derivatives: Structure, Properties, and Applications. *International Journal of Scientific Research in Science and Technology*. 11. 17-42. 10.32628/IJSRST24114141.
7. Pathak, Nandini & Rathi, Ekta & Kumar, Nitesh & Kini, Suvarna & Rao, Chamallamudi. (2019). A Review on Anticancer Potentials of Benzothiazole Derivatives. *Mini-Reviews in Medicinal Chemistry*. 19. 10.2174/1389557519666190617153213.
8. Sadhasivam, Gnanavel & Kulanthai, Kannan & Sowmiya, Rajamani & Perumal, Pachiappan. (2016). Synthesis, characterization, and anti-plasmodial activity of 2,6-substituted benzothiazole derivatives. *Bangladesh Journal of Pharmacology*. 11. 321. 10.3329/bjp.v11i2.24886.
9. Sarkar, Souvik & Siddiqui, Asim & Saha, Shubhra & De, Rudranil & Mazumder, Somnath & Banerjee, Chinmoy & Iqbal, Mohd Shameel & Nag, Shiladitya & Adhikari, Susanta & Bandyopadhyay, Uday. (2016). Antimalarial Activity of Small-Molecule Benzothiazole Hydrazones. *Antimicrobial Agents and Chemotherapy*. 60. AAC.01575-15. 10.1128/AAC.01575-15.
10. Tran, Linh & Tu, Vo & Dadam, Mohammad Najm & Abdul Aziz, Jeza & Duy, Tran & Ahmed, Hajer & Kwaah, Patrick & Hoang Nghia, Quoc & Truong, Van-Dat & Mizuta, Satoshi & Hirayama, Kenji & Nguyen, Huy. (2023). Antimalarial activities of benzothiazole analogs: A systematic review. *Fundamental & Clinical Pharmacology*. 38. 10.1111/fcp.12974.



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