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In-Vivo Evaluation of Benzothiazole Derivatives as Potential Anti-Cancer Agents

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ABSTRACT: This study investigates the in-vivo anti-cancer activity of synthesized benzothiazole derivatives. The anticancer potential of the synthesized compounds was assessed by subdividing the mice into groups, each receiving specific doses of the compounds under investigation. The results demonstrate a significant impact on both body weight and survival time, indicating the potential of benzothiazole derivatives as anti-cancer agents.

KEYWORDS: Benzothiazole, anti-cancer activity, efficacy.

I. INTRODUCTION

Cancer is the most significant, remarkably intricate and fatal disease that has become a major concern in contemporary medical science. It presents a significant challenge to the medical science community in the development of drugs for safer cancer treatment and cure. Heterocyclic compounds, including benzothiazole, hold considerable importance in organic chemistry and pharmaceutical development because of their varied roles. Benzothiazole and its derivatives have been thoroughly investigated for their prospective biological functions. The synthesis of benzothiazole derivatives remains a prominent research focus, with numerous synthetic methodologies established for their production. The advancement of innovative synthetic techniques and the alteration of current methodologies have facilitated the generation of new scaffolds with enhanced biological characteristics and specificity. The investigation of the pharmacological characteristics of novel benzothiazole derivatives remains a promising field of research, offering the possibility for novel drug and therapy development. Therefore, this study aims to evaluate the anti-cancer potential of benzothiazole derivatives.

II. RESEARCH METHODOLOGY

Benzothiazole derivatives: Five benzothiazole derivatives were studied for their anti-cancer activity. Following compounds were studies for their anti-cancer activity:

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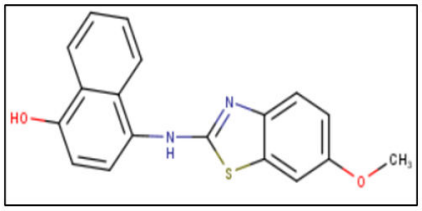
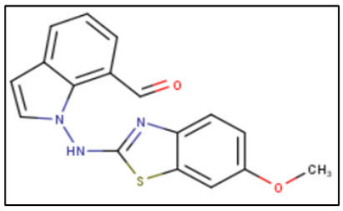
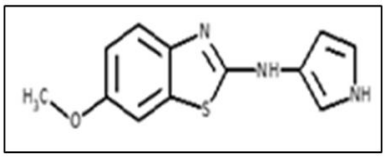
Fig 1: Compounds showing anti-cancer activity



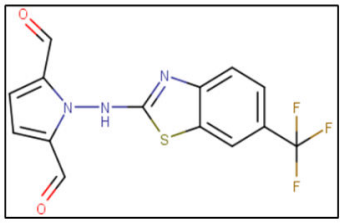
4-[(6-methoxy-1,3-benzothiazol-2-yl)amino]naphthalen-1-ol (Derivative A)



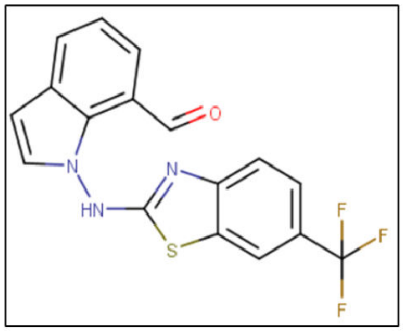
1-[(6-methoxy-1,3-benzothiazol-2-yl)amino]-1H-indole-7-carbaldehyde (DerivativeB)



6-methoxy-N-(1H-pyrrol-3-yl)-1,3-benzothiazol-2-amine (Derivative C)



1-{[6-(trifluoromethyl)-1,3-benzothiazol-2-yl]amino}-1H-pyrrole-2,5-dicarbaldehyde (Derivative D)



1-{[6-(trifluoromethyl)-1,3-benzothiazol-2-yl]amino}-1H-indole-7-carbaldehyde (Derivative E)

In Vivo anti-cancer activity: Female Swiss albino mice inoculated with Ehrlich ascites cancer (EAC) were tested for the antitumor effectiveness of synthesized compounds. Female Swiss albino mice, weighing between 25 and 30 grams, were kept for study. Cells of Ehrlich ascites carcinoma (EAC) was also obtained. The anticancer effectiveness of the compounds under investigation was evaluated. The mice were subdivided into groups based on the delivered compounds. At zero-day, mice were weighed and then received an intraperitoneal injection of 2.5×106 EAC cells per mouse. Following a period of 3 days, animals received doses of the desired compounds. On the 18th day, the mice were weighed. The mean survival time (MST) was also determined in each group. The impact of the specific formulations on the percentage changes in body weight is demonstrated in Table.

III. OBSERVATION

As shown in the results, Derivative A caused a 16.5% increase in body weight and had an MST of 33 days, suggesting limited effectiveness and significant tumor progression. Derivative B, with a 6.8% increase in body weight and an MST of 51 days, displayed some antitumor activity in comparison to the normal group. Derivative C led to a 19.3% increase in body weight and an MST of 28 days, indicating severe tumor growth and reduced survival time, which is less

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favorable compared to the control. Derivative D resulted in a 6.9% increase in body weight and an MST of 49 days, showing some effectiveness but still lower than the normal group. Derivative E, with a 14.1% increase in body weight and an MST of 35 days, demonstrated improved efficacy compared to some other derivatives, although not surpassing the normal group.

Overall, the MSTs of Derivatives A, B, C, D, and E varied, with Derivatives B, D and E showing relatively better outcomes than Derivative A and Derivative C. These variations in MSTs and body weight changes suggest that while some compounds exhibit potential for further development, others may require deeper research to enhance their antitumor effectiveness.

Table 1: Observed Anti-cancer Activity

Compound Administered	Change in body weight (%)	MST (Mean Survival Time) (days)
Normal Group	7.5	55
Derivative A	16.5	33
Derivative B	6.8	51
Derivative C	19.3	28
Derivative D	6.9	49
Derivative E	14.1	35

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

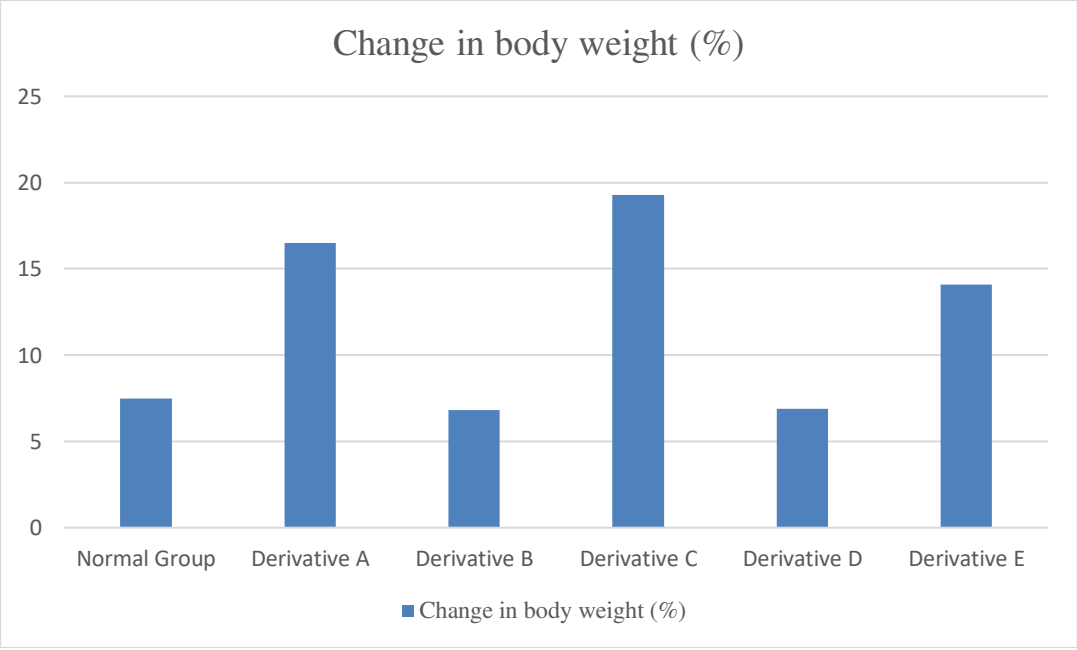

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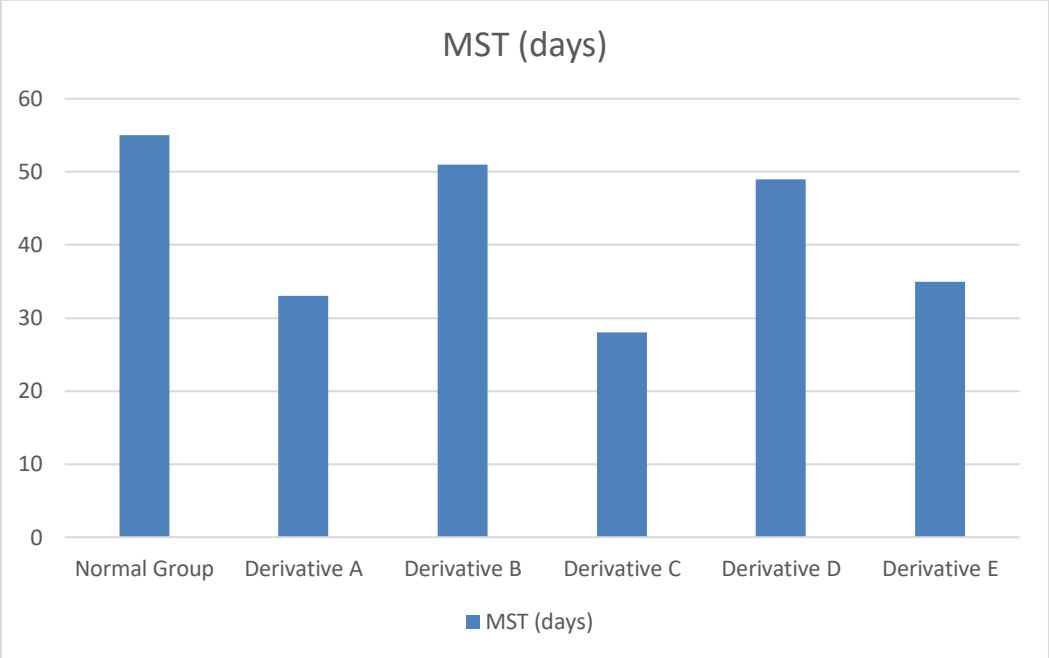
Fig 3: Observed Anti-cancer Activity (MST)



SAR study of both derivatives B and E revealed that compound featuring a benzothiazole ring fused with an indole ring can be designed to inhibit tubulin polymerization. The indole scaffold serves as the central structural framework, which binds to the colchicine-binding site on tubulin, disrupting microtubule formation. This inhibition of tubulin dynamics induces mitotic arrest and apoptosis, making Derivative B and E, promising anti-cancer agents. Also, derivative D is a benzothiazole-based compound featuring a pyrrole ring, designed for its potent anticancer activity. SAR studies of similar derivatives in previous studies have shown that the presence of pyrrole ring in the benzothiazole compound is crucial for anti-cancer activity.

IV. CONCLUSION

The study highlights the varying antitumor activity of the select benzothiazole derivatives. While Derivatives B, D and E display some potential for further exploration as anti-cancer agents, Derivatives A and C demonstrated limited efficacy and may require structural modifications to improve their therapeutic outcomes. These findings suggest that while certain benzothiazole derivatives exhibit promising antitumor activity, further research is needed to optimize their effectiveness and therapeutic application.

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