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Assessing the Anti-Diabetic Potential of Novel Benzothiazole Derivatives: An In-Vivo Approach

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ABSTRACT: The development of antidiabetic medications has consistently posed a significant challenge for medicinal chemists globally due to the rising prevalence of diabetes worldwide. In recent times, benzothiazole derivatives have garnered significant attention for their diverse pharmacological properties, including their potential in managing diabetes mellitus. This study aims to evaluate the in-vivo anti-diabetic activity of select benzothiazole derivatives.

KEYWORDS: Benzothiazole, anti-diabetic, efficacy.

I. INTRODUCTION

Diabetes, a metabolic illness, is becoming a significant concern for medicinal chemists worldwide. A recent estimate on global diabetes prevalence indicates that 592 million individuals will be affected by diabetes by 2035. In light of these alarming statistics, extensive research is being conducted globally to manage diabetes and its associated complications. Heterocyclic moieties are essential in the drug discovery process, serving as the core pharmacophore for the majority of current diabetes treatment options. Numerous heterocycles, including pyrazoles, thiazolidinones, pyrimidines, benzimidazoles, quinolones, and benzothiazoles, have been utilized for decades in the pursuit of potential anti-diabetic agents.

Benzothiazole (BTA) and its derivatives are significant heterocyclic chemicals, prevalent in natural products and pharmaceutical formulations. Innovative concepts are driving the advancement of BTA-containing pharmaceuticals that exhibit enhanced activity, reduced toxicity, and improved efficacy in disease diagnosis. Therefore, this aims to conduct in-vivo study on efficiency of benzothiazole derivatives as an anti-diabetic agent.

II. RESEARCH METHODOLOGY

Benzothiazole derivatives: Four benzothiazole compounds were tested for their anti-diabetic activity. Following benzothiazole derivatives were studied:

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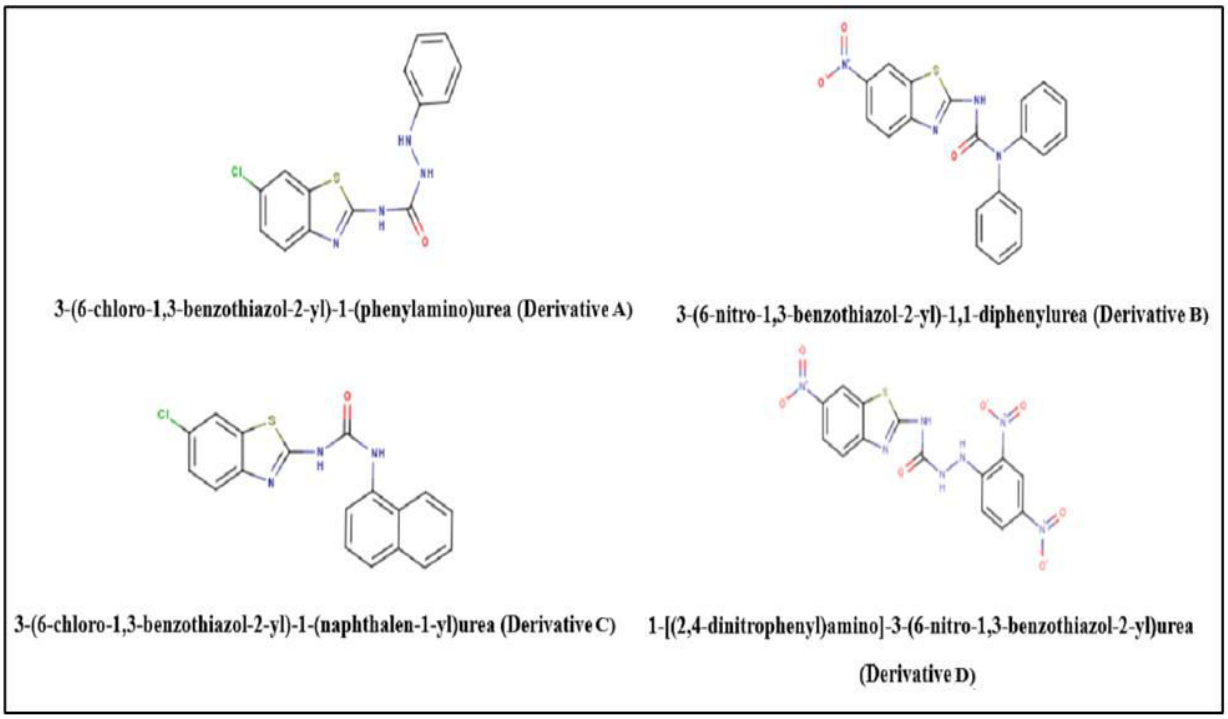
Fig 1: Compounds showing anti-diabetic activity



In Vivo anti-diabetic activity: Mature adult albino rats weighing 180-210g were acquired and kept at standard conditions of temperature and relative humidity, with a 12-hour light dark cycle. Complimentary water and commercial rat diet were supplied without restriction. The study used adult albino rats of either gender weighing between 180 and 210 grams. The animals were partitioned into groups. Alloxan was frequently employed as an animal model for experimental diabetes. Prior to the introduction of diabetes, the animals underwent a 12-hour fasting period with minor adjustments. A single dose of 140mg/kg body weight of Alloxan (ALX), freshly produced in 0.5% Tween 80, was delivered intraperitoneally. A diagnosis of diabetes was established by assessing blood glucose levels 5 days post-administration of ALX. Animals exhibiting a blood glucose level exceeding 200 mg/dl were classified as diabetic and included in the experiments. Different groups of rats then received doses of different compounds. All the experimental rats had an overnight fasting period. The subjects were monitored continually for any noticeable changes in behavior and signs of excessive activity, grooming, seizures, sedation, low body temperature, and death within the initial three-hour period. The animals were next subjected to continuous monitoring at regular intervals. Acute study blood samples were obtained from the retro-orbital plexus of each rat under moderate anesthesia at 0 and 4 hours, after administration. Level of blood glucose was determined using the enzymatic glucose oxidase technique. Calculation of the decrease in blood glucose level was performed relative to the original level.

III. OBSERVATION

The results indicated that the different compounds exhibited varying degrees of antidiabetic activity. Derivative A reduced the blood glucose level from 268.6 mg/dl to 177.5 mg/dl, corresponding to a 33.9% reduction. Derivative B lowered glucose from 275.4 mg/dl to 192.3 mg/dl, representing a 30.18% decrease. Derivative C demonstrated a reduction from 275.3 mg/dl to 178.2 mg/dl, yielding a 35.25% decrease in blood glucose levels. Finally, Derivative D showed the highest activity, reducing the blood glucose level from 265.3 mg/dl to 170.6 mg/dl, resulting in a 35.67% reduction. These findings suggest that the compounds, particularly Derivatives C and D, show promising antidiabetic

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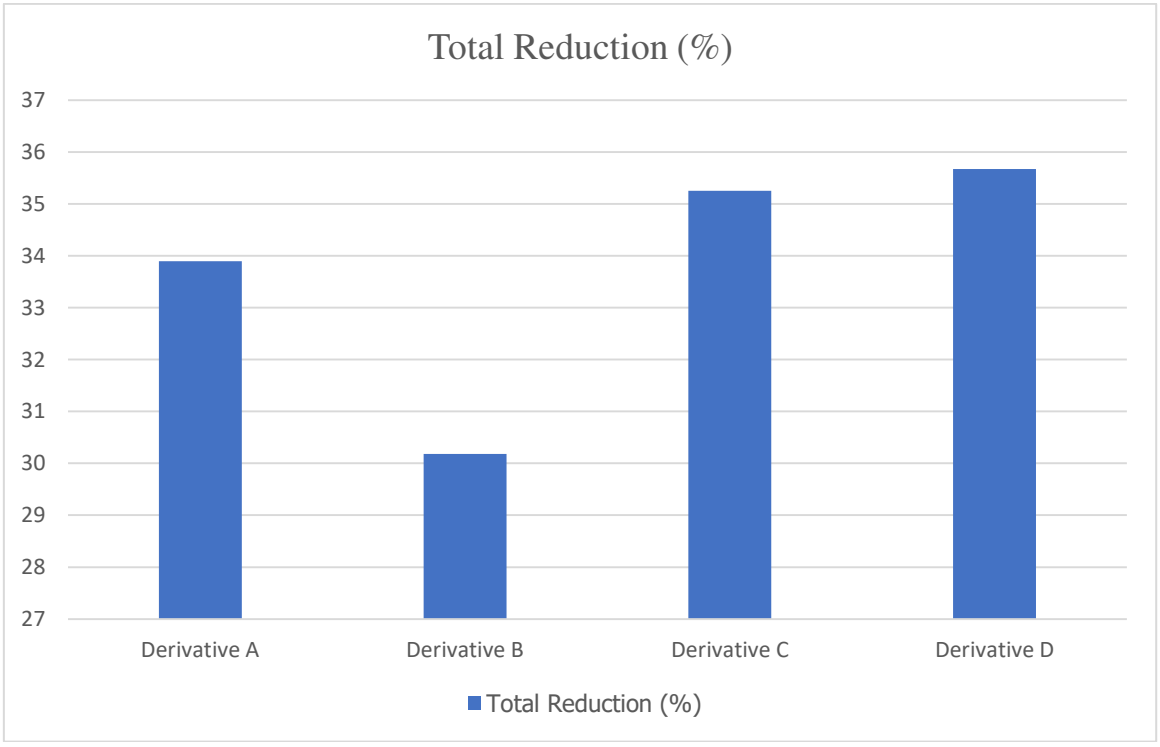
potential by significantly lowering blood glucose levels in diabetic rats. Further studies would be required to explore their mechanisms of action and to assess their long-term efficacy and safety.

Table 1: Observed Anti-diabetic Activity

Compound Administered	Blood Glucose Level (mg/dl)		Total Reduction (%)
	0h	4h	
Normal Group	85.34	96.34	-
Derivative A	268.6	177.5	33.89805
Derivative B	275.4	192.3	30.1808
Derivative C	275.3	178.2	35.25266
Derivative D	265.3	170.6	35.67309

Fig 2: Observed Anti-diabetic Activity



SAR study of different derivatives revealed that the naphthyl group enhance lipophilicity and receptor interactions for Derivative C and dinitrophenyl for Derivative 21 (contributing to strong electron-withdrawing effects, which may enhance binding affinity to enzymes like alpha-glucosidase for anti-diabetic activity).

IV. CONCLUSION

The study demonstrates that the tested benzothiazole derivatives exhibit varying degrees of anti-diabetic activity in diabetic rats. Among the compounds, Derivatives C and D showed the most pronounced glucose-lowering effects, with reductions of 35.25% and 35.67%, respectively. Derivatives A and B also displayed significant activity, reducing blood glucose levels by 33.9% and 30.18%. These results suggest that benzothiazole derivatives, particularly C and D, have promising potential as anti-diabetic agents. The ability of these compounds to significantly reduce blood glucose levels

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highlights their therapeutic promise for managing diabetes. Further research is necessary to investigate their long-term safety and efficacy, and assess their potential for clinical applications in diabetes management.

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