

## Research Article



## In-vivo Antidiabetic Activity of Novel N-substituted Thiazolidinedione Derivative in Streptozotocin Induced Diabetic Albino Wister Rats

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### ABSTRACT

The present study was focused to evaluate *in-vivo* anti-diabetic activity of novel N- substituted thiazolidinedione derivative in the streptozotocin diabetic rats. Diabetes was induced in overnight fasted rats by single intraperitoneal injection of streptozotocin (60 mg/kg). Blood glucose levels were measured 7 days after the streptozotocin injection and blood glucose levels and body weight are monitored on 0<sup>th</sup>, 1<sup>st</sup>, 7<sup>th</sup> and 15<sup>th</sup> day. The statistical data indicated that the novel N- substituted thiazolidinedione derivative significantly decrease the level of blood glucose in streptozotocin induced rats. It was found that novel derivative showed highly significant decrease in the blood glucose levels when compared to the control STZ induced diabetic animals which was compared with the standard drug Pioglitazone (36 mg/kg).

**Keywords:** Thiazolidinedione, Pioglitazone, Streptozotocin induced diabetic activity, Diabetes Mellitus.

### QUICK RESPONSE CODE →

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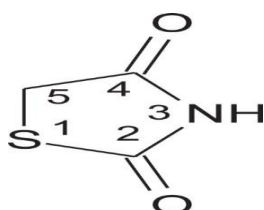


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### INTRODUCTION

According to WHO reports; 30 million people were affected from diabetes in 1985 which increased to 185 million in 2000 and expected to double by 2030. These epidemic calculations put a demand towards the development of more potent and efficacious agents to control diabetes. Many drugs have been approved from thiazolidinedione class for the treatment of diabetes like Rosiglitazone, Pioglitazone, Ciglitazone and many more. Though they show additive effects, they are prone to show toxicity.

2, 4-thiazolidinedione<sup>1</sup> consists of a five membered thiazolidine ring with carbonyl group at 2 and 4 positions. Variable substitutions occur at 3 and 5 positions, but substitution at 2 cause changes in structure and properties of thiazolidinedione.



Thiazolidinediones are found to exhibit wide range of pharmacological activities such as anti-hyperglycaemic, antiviral, anticancer, antimicrobial, aldose reductase

inhibitors, etc. The biological activities associated with TZD derivatives are due to the binding of molecule with PPAR gamma (Peroxisome Proliferators Gamma Activated Receptor).

### MATERIALS AND METHODS

#### Methodology for Synthesis<sup>2</sup>

##### Step 1: Synthesis of Thiazolididione

In a 250ml three-necked flask, a solution containing 0.6mol of chloroacetic acid in 60mL of water and 0.6mol of thiourea was dissolved in 60mL of water. The mixture was stirred until the white precipitate was formed. 60ml of conc. hydrochloric acid was slowly added to the contents of flask. After dissolving the precipitates, reaction mixture was stirred and then refluxed for 10-12hrs at 100- 110°C, on cooling the contents of flask were solidified to a mass of clusters of white needles. The product was filtered and washed with water to remove traces of hydrochloric acid and dried. It was recrystallised from ethanol.

##### Step 2: Synthesis of Thiazolidinedione Derivative

4-(benzyloxy) benzaldehyde (0.2M) in DMF was added into a solution of 2, 4-thiazolidinedione (0.1M) in DMF, under stirring. The reaction mixture was stirred at room temperature for 15 min. To the solution, diethylamine DMF was added drop wise and reflux for 12 hours. After 12 hours the reaction mixture was poured in an ice cold water and filtered off and wash with hot water. Finally it was recrystallised from chloroform, ethanol to give final compound.

#### Animals

Albino rats (Wistar strain) were used to carry out the activities. The animals had free access to standard commercial diet and water *ad libitum* and were housed in



cages under standard laboratory conditions i.e.; 12:12 hour light or dark cycle at 25±20°C. The experiments were carried out as per the guidelines of CPCSEA, New Delhi, India and approved by the Institutional Animal Ethical Committee (IAEC Number.: PCP/IAEC/2019-1/1).

**In- vivo anti-diabetic activity**

Streptozotocin induced Diabetic study<sup>3</sup>

Diabetes was induced in overnight fasted rats by single intraperitoneal injection of streptozotocin (60 mg/kg). Blood glucose levels were measured 7 days after the streptozotocin injection and rats with fasting blood glucose levels greater than 200 mg/dl were considered to be diabetic used in the experiment.

Experimental design

5 groups of rats were used to study and each group consists of 6 rats.

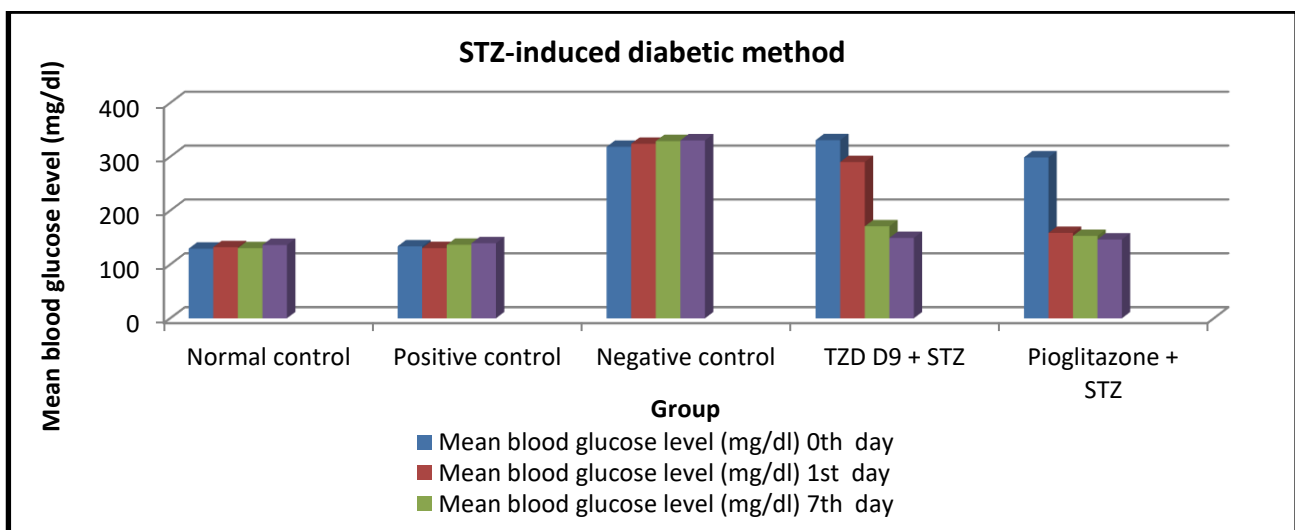
- Group I: untreated group (normal control).

- Group II: Positive control (0.1 M citrate buffer is given).
- Group III: Disease control induced with 60 mg/kg of Streptozotocin (I.P).
- Group IV: Diabetic rats were treated with TZD D9 60 mg/kg.
- Group V: Diabetic rats were treated with Pioglitazone 36 mg/kg body weight.

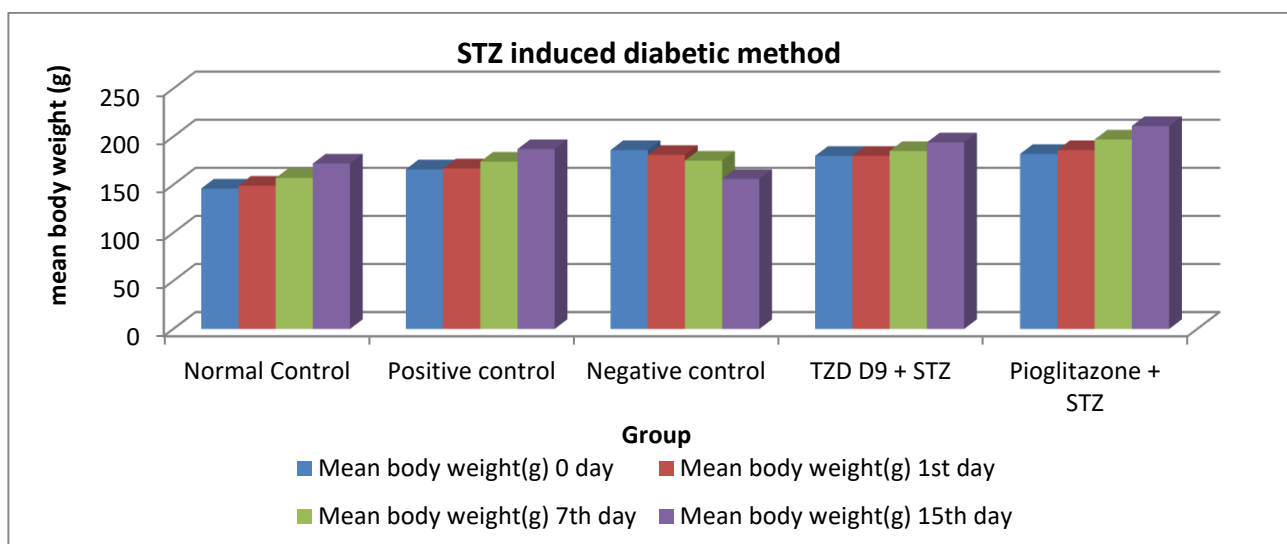
Treatment of experimental animals with synthesised TZD derivatives was initiated after 7 days streptozotocin injection, and blood glucose levels and body weight are monitored on 0<sup>th</sup>, 1<sup>st</sup>, 7<sup>th</sup> and 15<sup>th</sup> day.

**Statistical analysis**

Value are expressed as mean ± SEM from six observations. Statistical analysis was done by one-way anova followed by dunnett’s t-test.



**Figure 1:** Effect of TZD derivative on blood glucose level in STZ induced diabetic rat



**Figure 2:** Effect of TZD D9 on body weight in STZ-induced diabetic rats.

## RESULTS AND DISCUSSION

### *In vivo* antidiabetic activity

#### *Effect of novel compound on Blood Glucose Level in STZ-Induced Diabetic Rats.*

Blood glucose level of all the animals were recorded as per the study design.

#### *Effect of novel compounds on Body Weight in STZ-Induced Diabetic Rats*

Body weights of all the animals were recorded as per the study design. Average weekly body weight of the animal showed a gradual increase in body weight in the animals of all five groups.

## CONCLUSION

The current study found that TZD derivative 4(benzyloxy) benzaldehyde showed highly significant decrease in the blood glucose levels when compared to the control STZ induced diabetic animals which was compared with the standard drug Pioglitazone (36 mg/kg). N- Substituted thiazolidinedione derivative was also found to be safe at the oral dose of 60mg/kg body weight in rats.

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**Conflict of Interest:** None declared.

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