

# The Effectiveness of Ethanol Extract of *Terminalia catappa* L. Leaves on Blood Glucose Levels and Pancreatic Histopathology in Streptozotocin-Induced Male Wistar Rats.

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## ABSTRACT

Diabetes mellitus is a condition in which the body experiences an increase in blood glucose levels but is unable to produce energy effectively. This condition is commonly known as hyperglycemia, which occurs due to impaired insulin secretion, decreased insulin sensitivity, or a combination of both. Uncontrolled hyperglycemia in patients can lead to serious damage to various body systems. In the pancreas, it may cause a reduction in both the number and size of the islets of Langerhans, particularly affecting the insulin-producing beta cells. This condition is characterized by a decrease in the cellular population within the islets of Langerhans compared to a normal pancreas, along with a reduction in the number of alpha, beta, and delta cells.

Ketapang (*Terminalia catappa* L.) leaves contain antioxidant compounds known to act as free radical scavengers. These antioxidants help prevent conditions in which the number of free radicals in the body exceeds the body's capacity to neutralize them, leading to oxidative stress. The main bioactive components found in Ketapang (*Terminalia catappa* L.) leaves include flavonoids, tannins, terpenoids, and saponins. Flavonoids, a class of polyphenolic compounds, are known for their pharmacological properties, particularly their antidiabetic activity. Based on this background, the present study aims to evaluate the effectiveness of the ethanol extract of Ketapang (*Terminalia catappa* L.) leaves on blood glucose levels and pancreatic histology in streptozotocin-induced male Wistar rats.

**Keywords:** Provide 3-5 appropriate keywords suitable for your manuscript.

## INTRODUCTION

From year to year, *Diabetes mellitus* has become an increasing global health burden for many countries. According to the latest data from the NCD Risk Factor Collaboration (2022), approximately 828 million people worldwide are living with diabetes, and more than 95% of them suffer from type 2 diabetes. Based on recent projections, the prevalence of diabetes in the United States is estimated to reach 10.8% by 2050 (Mlynarska et al., 2025). In Indonesia, the number of people aged 20–79 years living with *Diabetes mellitus* reached approximately 10.7 million in 2019. According to recent data, the prevalence of *Diabetes mellitus* in Indonesia has increased by 8.5% (Melviani et al., 2025). *Diabetes mellitus* is classified as a metabolic disorder characterized by elevated blood glucose levels resulting from impaired

insulin activity in the bloodstream (Silalahi, 2019). In this condition, glucose cannot be properly utilized by cells because it cannot be converted into glucose-6-phosphate.

*Ketapang* (*Terminalia catappa* L.) leaves contain antioxidant compounds known to function as free radical scavengers, which help prevent conditions in which the number of free radicals in the body exceeds its capacity to neutralize them, leading to *oxidative stress* (Iheagwam et al., 2021). *Ketapang* (*Terminalia catappa* L.) leaves contain antioxidant compounds known to function as free radical scavengers, which help prevent conditions in which the number of free radicals in the body exceeds its capacity to neutralize them, leading to *oxidative stress* (Iheagwam et al., 2021). The bioactive components found in *Ketapang* (*Terminalia catappa* L.) leaves include flavonoids, tannins, terpenoids, and saponins. Flavonoids exhibit a wide range of pharmacological activities, including anti-inflammatory, anticancer, antiviral, and antidiabetic effects, through various cellular signaling pathways. One of the flavonoid derivatives, rutin, has been reported to possess significant antidiabetic activity (Rachmawati, 2022).

This study has important implications for the treatment of diabetes-related diseases and enhances the understanding of the potential benefits of medicinal plants in alternative therapy. This study contributes to a deeper understanding of the relationship between *Diabetes mellitus* (DM) and blood glucose levels. It may serve as a foundation for developing more effective disease management strategies for patients with DM and for exploring the use of natural plant-derived compounds, such as flavonoids found in *Ketapang* (*Terminalia catappa* L.) leaves, as antioxidant agents. This will further strengthen the concept of using herbal medicines or natural therapies as alternative options in the management of DM-related diseases.

## METHODS

This study employed a *true experimental design*, specifically using a *Post-Test Only Control Group Design*. This design involves observation of both the control and treatment groups only after the intervention has been administered.

The samples in this study were male *Wistar* rats weighing between 180–250 g and aged 2–3 months. The inclusion criteria for the experimental animals were male *Wistar* rats with body weights ranging from 180–250 g, aged 2–3 months, physically healthy, free from anatomical abnormalities, and not previously used in any experimental study.

The experimental animals were divided into four groups, with a minimum of five rats per group, resulting in a total of 20 rats used in the study. The allocation of experimental animals into the groups was performed randomly.

The instruments utilized in this study included a maceration apparatus, filtration system, rotary evaporator, evaporating dish, water bath, volumetric flasks (10 mL, 25 mL, and 100 mL), test tubes with racks, *BioHit* micropipette (1000 µL), graduated pipette, spatula, vials, incubator, pH meter, cuvettes, centrifuge with centrifuge tubes, UV–Vis spectrophotometer, and beakers. The primary material used was *Ketapang* leaves (*Terminalia catappa* L.).

The extraction of *Terminalia catappa* L. leaves was carried out using the maceration technique with 96% ethanol as the solvent. The plant material was soaked for seven days under constant agitation to ensure optimal compound dissolution. The resulting extract was then filtered to obtain a clear filtrate, which was subsequently concentrated using a rotary vacuum evaporator at a temperature of 50°C. The concentrated extract was further subjected to freeze-drying to produce a crude, dark-colored extract.

This study was conducted starting on July 20, 2025, at the Laboratory of Universitas Prima Indonesia.

## RESULTS

This study utilized 20 male *Wistar* rats that were induced to develop diabetes. The animals were randomly divided into four treatment groups, with five rats in each group, as follows:

**Table 1. Treatment Groups**

Group 1	No treatment
Group 2	Rats induced with streptozotocin at a dose of 35 mg/kg BW and treated with <i>Terminalia catappa L.</i> leaf extract at a dose of 50 mg/kg BW
Group 3	Rats induced with streptozotocin at a dose of 35 mg/kg BW and treated with <i>Terminalia catappa L.</i> leaf extract at a dose of 100 mg/kg BW
Group 4	Rats induced with streptozotocin at a dose of 35 mg/kg BW and treated with <i>Terminalia catappa L.</i> leaf extract at a dose of 150 mg/kg BW

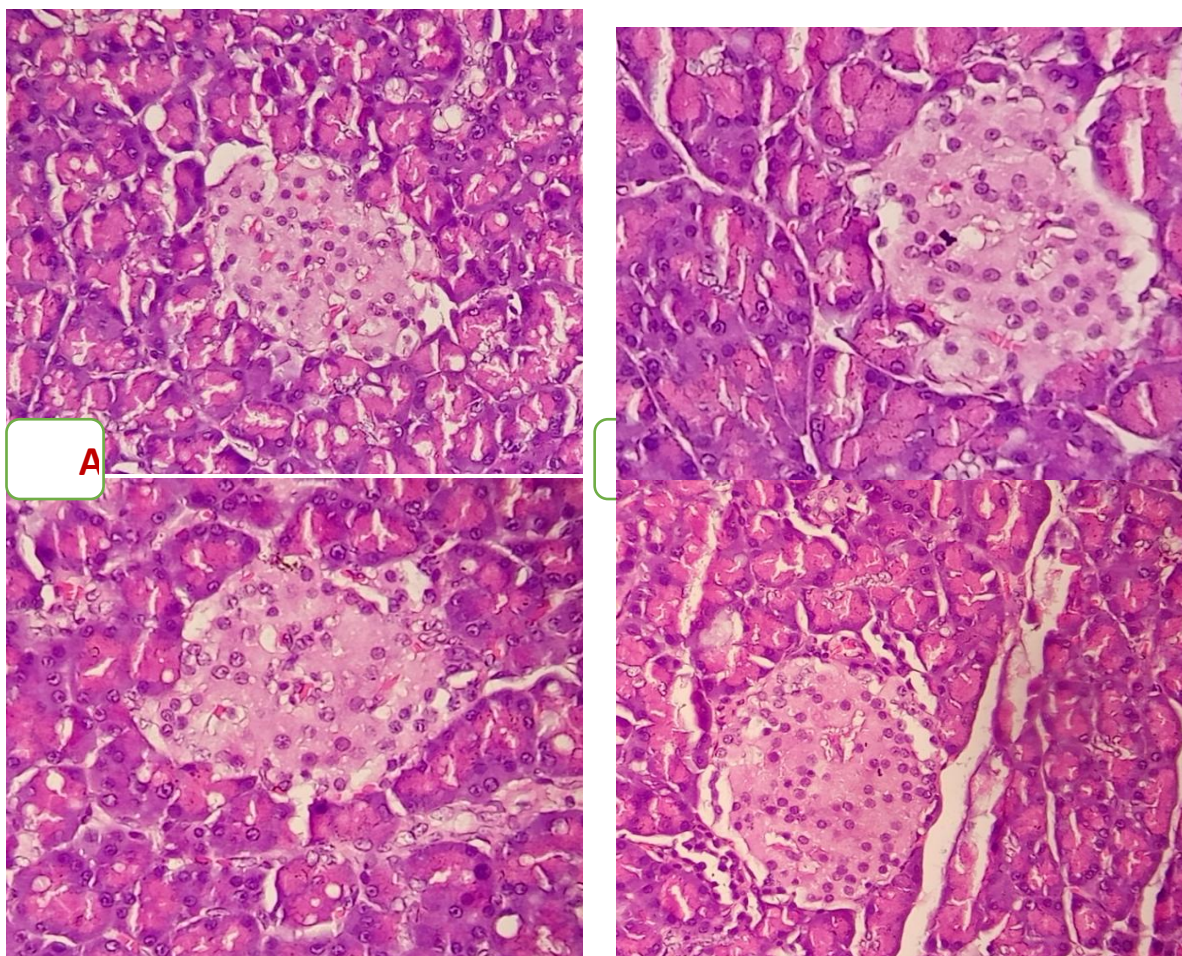
Blood glucose levels were measured on day 0 (before treatment), day 7 (after *streptozotocin* induction), and day 14 (after administration of *Terminalia catappa L.* leaf extract). On day 21, all rats were sacrificed, and histopathological examinations of the pancreas were performed. The results of blood glucose measurements were analyzed by comparing the mean blood glucose levels before and after treatment.

**Table 2. Mean Blood Glucose Levels Before and After Treatment**

Parameter	p-value
Blood glucose level before <i>streptozotocin</i> induction	0,019
Blood glucose level after <i>streptozotocin</i> induction	0,001
Blood glucose level after administration of <i>Terminalia catappa L.</i> leaf extract	0,001

The homogeneity test (Levene's test) in this study showed a p-value of 0.227 ( $>0.05$ ), indicating that the variances among the groups were homogeneous. The ANOVA test revealed a p-value of 0.019 ( $<0.05$ ), demonstrating a statistically significant difference in blood glucose levels among the groups before *streptozotocin* (STZ) induction.

**Figure 1. Histological structure of the pancreas (Hematoxylin–Eosin staining, 400× magnification)**



**Description:** Figure (A) illustrates the histological architecture of the pancreatic tissue in the control group (without treatment). Figure (B) depicts the histological structure of the pancreatic tissue in rats induced with streptozotocin at a dose of 35 mg/kg body weight and subsequently administered *Terminalia catappa* leaf extract at a dose of 50 mg/kg body weight. Figure (C) presents the histological architecture of the pancreatic tissue in rats induced with streptozotocin at a dose of 35 mg/kg body weight and subsequently administered *Terminalia catappa* leaf extract at a dose of 100 mg/kg body weight. Figure (D) shows the histological structure of the pancreatic tissue in rats induced with streptozotocin at a dose of 35 mg/kg body weight and subsequently administered *Terminalia catappa* leaf extract at a dose of 150 mg/kg body weight. Based on the observations, a decrease in the number of Langerhans islet cells was noted in the treatment groups. Histopathological examination of the pancreatic tissue in the group treated with streptozotocin (35 mg/kg BW) and Ketapang leaf extract (150 mg/kg BW) demonstrated notable improvement in the morphology and integrity of the Langerhans islet cells compared to the other treatment groups.

These findings are in agreement with previous studies, which reported that *Terminalia catappa* L. extract possesses antioxidative and anti-inflammatory properties capable of restoring redox balance and mitigating inflammation in rats induced with low-dose streptozotocin. A previous literature review has also elaborated on the potential mechanisms through which *Terminalia catappa* L. exerts its antidiabetic and antihyperlipidemic effects. The extract of *Terminalia*

*catappa* L. also prevents progressive damage to pancreatic  $\beta$ -cells by inhibiting protein glycosylation (Behl & Kotwani, 2017).

## CONCLUSION

Based on the results of this study, it can be concluded that the administration of ethanol extract of *Terminalia catappa* L. leaves demonstrated a significant effect in improving blood glucose levels and was capable of restoring the pancreatic histological structure from damage.

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