



IN VIVO ANTIHYPERGLYCEMIC EVALUATION OF ETHANOLIC SEED EXTRACT OF SYZYGIUM CUMINI IN STREPTOZOTOCIN – INDUCED DIABETIC RATS

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ABSTRACT

The present study was undertaken to evaluate the antioxidant and antihyperglycemic activity of the ethanolic seed extract of *Syzygium cumini* using in-vitro and in-vivo experimental models. The seeds of *Syzygium cumini* were collected, authenticated, and subjected to morphological, organoleptic, and physicochemical evaluation to ensure the quality and identity of the plant material. Preliminary phytochemical screening of the ethanolic seed extract revealed the presence of various bioactive constituents such as alkaloids, flavonoids, tannins, glycosides, terpenoids, and phenolic compounds. The antioxidant potential of the extract was evaluated by the DPPH free radical scavenging assay, which showed concentration-dependent activity with an IC₅₀ value of approximately 71.74 µg/ml. The in-vitro antihyperglycemic activity was assessed using the α-amylase inhibition assay, where the extract

exhibited moderate enzyme inhibitory activity compared with the standard drug acarbose. Acute toxicity studies performed according to OECD guideline 423 indicated that the extract was safe up to a dose of 2000 mg/kg body weight and doses of 200 mg/kg and 400 mg/kg were selected for in-vivo studies. The antihyperglycemic activity was evaluated using the streptozotocin (STZ)-induced diabetic rat model. Treatment with the extract significantly

reduced blood glucose levels in diabetic rats in a dose-dependent manner. The extract also improved serum biochemical parameters such as total cholesterol, triglycerides, HDL, and LDL levels and prevented diabetes-induced body weight loss. Histopathological examination of pancreatic tissue revealed protective and regenerative effects on pancreatic β -cells. Overall, the results indicate that the ethanolic seed extract of *Syzygium cumini* possesses significant antioxidant and antihyperglycemic properties, supporting its traditional use in the management of diabetes mellitus and suggesting its potential as a natural therapeutic agent.

KEYWORDS: *Syzygium cumini*, Ethanolic seed extract, Antihyperglycemic activity, Streptozotocin-induced diabetes, DPPH antioxidant assay, α -amylase inhibition, Phytochemical screening.

INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The condition leads to disturbances in carbohydrate, lipid, and protein metabolism and can result in long-term damage to various organs, particularly the eyes, kidneys, nerves, heart, and blood vessels. The hormone insulin, produced by the β -cells of the pancreas, plays a central role in regulating blood glucose levels by facilitating the uptake of glucose into cells for energy production or storage. When insulin production is inadequate or when the body becomes resistant to its action, glucose accumulates in the bloodstream, leading to hyperglycemia and the clinical manifestations of diabetes.

The history of diabetes dates back thousands of years. The earliest description of the disease can be traced to ancient Egyptian medical manuscripts around 1500 BCE, where a condition characterized by excessive urination was documented. Later, the Greek physician Aretaeus of Cappadocia described the disease and used the term “diabetes,” meaning “to pass through,” referring to excessive urination. The term “mellitus,” meaning “honey-sweet,” was later added by the British physician Thomas Willis in the 17th century after observing that the urine of affected individuals had a sweet taste due to the presence of glucose. A major breakthrough in the treatment of diabetes occurred in 1921 when Frederick Banting and Charles Best discovered insulin, which revolutionized diabetes management and significantly improved patient survival. Since then, extensive research has been conducted to understand the pathophysiology of diabetes and to develop effective therapeutic strategies.

AIM AND OBJECTIVES

➤ AIM

To evaluate the antihyperglycemic potential of ethanolic seed extract of *Syzygium cumini* in Streptozotocin-induced diabetic rats through in-vivo experimental studies.

➤ OBJECTIVES

1. To collect, authenticate, and prepare the ethanolic seed extract of *Syzygium cumini*.
2. To perform preliminary phytochemical analysis of the extract.
3. To evaluate the *in-vitro* antioxidant activity using the 2,2-Diphenyl-1-picrylhydrazyl (DPPH) assay.
4. To assess the *in-vitro* antihyperglycemic activity by α -amylase inhibition assay.
5. To induce diabetes in experimental rats using Streptozotocin (STZ).

MATERIALS & EQUIPMENTS

Material

Table: Materials Used and Their Sources.

Sr. No	Name	Grade	Model & Make / Source
1	Plant material (e.g., <i>Syzygium cumini</i> seeds)	Crude	Collected from local area / authenticated by Botanist
2	Ethanol	Analytical Grade (AR)	SD Fine Chemicals
3	Methanol	Analytical Grade (AR)	HiMedia
4	Distilled water	Laboratory Grade	In-house Laboratory
5	Hydrochloric acid	Analytical Grade	Merck
6	Sulfuric acid	Analytical Grade	Merck
7	Ferric chloride	Analytical Grade	HiMedia
8	Dragendorff's reagent	Analytical Grade	HiMedia
9	Mayer's reagent	Analytical Grade	HiMedia
10	Wagner's reagent	Analytical Grade	HiMedia
11	Benedict's reagent	Analytical Grade	HiMedia
12	Molisch reagent	Analytical Grade	HiMedia
13	Lead acetate	Analytical Grade	Merck
14	Sodium hydroxide	Analytical Grade	Merck
15	1,1-Diphenyl-2-picrylhydrazyl (DPPH)	Analytical Grade	Sigma-Aldrich
16	α -Amylase enzyme	Analytical Grade	Sigma-Aldrich
17	Starch solution	Analytical Grade	HiMedia
18	Streptozotocin (STZ)	Analytical Grade	Sigma-Aldrich
19	Glucose estimation kit	Diagnostic Grade	Span Diagnostics
20	Standard drug Metformin	Pharmaceutical Grade	Trimurti pharmaceuticals

Equipment

Table: Equipment Used and Their Makers.

Sr. No	Equipment	Model & Make
1	Analytical balance	Shimadzu
2	Soxhlet extraction apparatus	Borosil Glass Works
3	Hot air oven	Labline
4	Rotary evaporator	Buchi
5	Water bath	Remi Instruments
6	UV-Visible Spectrophotometer	Shimadzu
7	Centrifuge	Remi Instruments
8	pH meter	Elico Instruments
9	Magnetic stirrer	Remi Instruments
10	Micropipettes	Eppendorf
11	Animal weighing balance	Citizen
12	Glucometer	Accu-Chek
13	Mortar and pestle	Borosil

In-vivo Pharmacological study^[126-149]

Procurement and Maintenance of Experimental Animals

Healthy adult Wistar albino rats of either sex weighing between 150–200 g were selected for the present study to evaluate the antihyperglycemic activity of the ethanolic seed extract of *Syzygium cumini*. The animals were procured from a registered breeder approved by the Institutional Animal Ethics Committee (IAEC) affiliated with Shri Wagheshwar Gramvikas Pratishthan's Pharate Patil College of Pharmacy, Mandavgan Pharata, Maharashtra, India. The use of healthy animals of similar age and body weight ensured uniformity and reliability in the experimental results.

After procurement, the animals were housed in clean polypropylene cages under standard laboratory conditions. The environmental parameters were maintained at a temperature of $25 \pm 2^\circ\text{C}$, relative humidity of 50–60%, and a 12-hour light–dark cycle throughout the experimental period. These controlled conditions were maintained to minimize stress and to ensure normal physiological functioning of the animals.

The animals were provided with a standard laboratory pellet diet and clean drinking water ad libitum. Prior to the commencement of the experiment, the animals were allowed to acclimatize to the laboratory conditions for one week. This acclimatization period helped stabilize their physiological state and reduced stress-related variations during the study.

Before induction of diabetes and administration of the test extract, the animals were subjected

to an overnight fasting period of approximately 12 hours, while water was allowed freely. All experimental procedures were carried out in accordance with the ethical guidelines of the Committee for the Purpose of Control and Supervision of Experiments on Animals, Government of India, and the study protocol was approved by the Institutional Animal Ethics Committee. The ethanolic seed extract of *Syzygium cumini* and the standard drug were administered orally using an oral gavage tube to ensure accurate and consistent dosing during the experimental period.



Figure: Wistar Rats and their maintenance.

Acute Toxicity Study and Dose Selection^[125-130]

Acute Toxicity Study (OECD Guideline 423)

The acute oral toxicity study of the ethanolic seed extract of *Syzygium cumini* was performed according to the **Organisation for Economic Co-operation and Development Guideline 423 (Acute Toxic Class Method)** to determine the safe dose range of the extract.

Healthy adult **Wistar albino rats** of either sex weighing between **150–200 g** were used for the study. The animals were fasted overnight with free access to water prior to the administration of the test extract. The ethanolic seed extract of *Syzygium cumini* was administered orally using an oral feeding needle.

Initially, a **single dose of 2000 mg/kg body weight** of the extract was administered to three rats. The animals were observed continuously during the first **4 hours** after administration for any behavioral changes or signs of toxicity such as tremors, convulsions, salivation, diarrhea, lethargy, sleep, or coma. Further observations were carried out periodically during the first **24 hours** and daily thereafter for a period of **14 days**.

During the observation period, mortality, behavioral changes, body weight variations, and

any signs of toxicity were carefully recorded. If no mortality or significant toxic symptoms were observed at the tested dose, the extract was considered safe.

Dose Selection^[131-135]

Based on the results obtained from the acute toxicity study, the **therapeutic doses for pharmacological evaluation** were selected as **fractions of the maximum safe dose**. Generally, **1/10th and 1/5th of the maximum tolerated dose** were selected for experimental studies.

Since the extract did not produce any mortality at **2000 mg/kg**, the doses selected for the antihyperglycemic study were:

- **Low dose:** 200 mg/kg body weight
- **High dose:** 400 mg/kg body weight

These doses were administered orally to experimental animals for evaluating the **antihyperglycemic activity of the ethanolic seed extract of *Syzygium cumini***.

Preparation of Streptozotocin (STZ) Solution and Citrate Buffer^[140-42]

Preparation of Citrate Buffer (0.1 M, pH 4.5)

Citrate buffer was prepared using **citric acid and trisodium citrate** to maintain the required acidic pH necessary for dissolving Streptozotocin.

Procedure

Solution A

- Dissolve **2.1 g of citric acid monohydrate** in **100 mL distilled water**.

Solution B

- Dissolve **2.94 g of trisodium citrate dihydrate** in **100 mL distilled water**.
- The required pH (**4.5**) was obtained by mixing appropriate volumes of solution A and solution B while monitoring with a **pH meter**.
- The prepared buffer solution was stored under refrigerated conditions until use.

Preparation of Streptozotocin Solution

Streptozotocin (STZ) is highly unstable in aqueous solutions and therefore must be prepared freshly just before administration.

Procedure:

- The required amount of **Streptozotocin** was accurately weighed under cold conditions.
- The compound was dissolved in freshly prepared **cold citrate buffer (0.1 M, pH 4.5)**.
- The solution was gently mixed to obtain a clear solution.
- The STZ solution was kept on **ice and protected from light** to prevent degradation.
- The prepared solution was administered **intraperitoneally to rats at a dose of 50–60 mg/kg body weight** within a few minutes of preparation.

Experimental Timeline for 21-Day Antihyperglycemic Study^[131-138]

The experimental protocol for evaluating the antihyperglycemic activity of the ethanolic seed extract of *Syzygium cumini* in STZ-induced diabetic rats was conducted over **21 days** as follows:

Figure 7.2: ethanolic seed extract of *Syzygium cumini* in STZ-induced diabetic rats was conducted over 21 days

Day	Experimental Activity
Day –7 to Day 0	Acclimatization of experimental animals to laboratory conditions
Day 0	Overnight fasting of animals
Day 1	Induction of diabetes by intraperitoneal injection of STZ
Day 2	Administration of 5% glucose solution to prevent hypoglycemic shock
Day 3	Measurement of fasting blood glucose and confirmation of diabetic rats
Day 3	Random grouping of animals into experimental groups
Day 3–21	Daily oral administration of plant extract and standard drug
Day 7	Measurement of blood glucose level
Day 14	Measurement of blood glucose level
Day 21	Final blood glucose estimation and biochemical analysis
Day 21	Collection of blood samples and organ tissues for further evaluation

In-Vivo Antihyperglycemic Activity of Ethanolic Seed Extract of *Syzygium cumini* in Streptozotocin (STZ)-Induced Diabetic Rats^[126-145]**Principle**

The **Streptozotocin (STZ)-induced diabetic rat model** is widely used for evaluating the antihyperglycemic activity of plant extracts and synthetic drugs. Streptozotocin is a diabetogenic agent that selectively destroys the insulin-producing **β -cells of the pancreatic islets of Langerhans**, leading to reduced insulin secretion and persistent hyperglycemia. Administration of STZ results in experimental diabetes that resembles human diabetes mellitus in terms of metabolic alterations.

In this method, diabetes is induced in experimental animals by a single intraperitoneal

injection of STZ. The antihyperglycemic potential of the ethanolic seed extract of *Syzygium cumini* is then evaluated by monitoring changes in blood glucose levels after treatment with the extract and comparing them with a standard antidiabetic drug.

Experimental Animals

Healthy adult **Wistar albino rats** of either sex weighing approximately **150–200 g** were used for the study. The animals were procured from a **CPCSEA-approved animal house**. They were housed in standard polypropylene cages under controlled environmental conditions of **temperature (22 ± 2°C), relative humidity (55–65%), and a 12-hour light/dark cycle**.

The animals were provided with **standard laboratory pellet diet and water ad libitum**. Before the initiation of the experiment, the animals were acclimatized to laboratory conditions for **one week**. All experimental procedures were conducted according to the guidelines of the **Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA)**, Government of India, and were approved by the **Institutional Animal Ethics Committee (IAEC)**.

Induction of Experimental Diabetes

Experimental diabetes was induced in overnight-fasted rats by a **single intraperitoneal injection of Streptozotocin (STZ)** dissolved in freshly prepared **0.1 M citrate buffer (pH 4.5)** at a dose of **50–60 mg/kg body weight**. After STZ administration, the animals were provided with **5% glucose solution for 24 hours** to prevent initial drug-induced hypoglycemic shock.

After **72 hours**, fasting blood glucose levels were measured using a glucometer by collecting blood samples from the tail vein. Rats showing **fasting blood glucose levels above 250 mg/dL** were considered diabetic and selected for further experimental studies.

Experimental Design and Animal Grouping

The animals were randomly divided into different groups, each consisting of **six rats (n = 6)**.

Table: Experimental Design and Animal Grouping

Group	Treatment
Group I	Normal control (received normal saline)
Group II	Diabetic control (STZ-induced diabetic rats without treatment)
Group III	Standard drug group (STZ + Metformin or Glibenclamide)
Group IV	Test group I (STZ + <i>Syzygium cumini</i> ethanolic seed extract – low dose)

Group V	Test group II (STZ + <i>Syzygium cumini</i> ethanolic seed extract – high dose)
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The ethanolic seed extract was administered orally using an oral feeding needle at selected dose levels (for example **200 mg/kg and 400 mg/kg body weight**) for a period of **21 days**.

Animal Grouping and Dose Calculation

Table: Experimental Animal Grouping for Antihyperglycemic Study.

Group	Treatment	Dose	Route of Administration	Number of Animals
Group I	Normal Control (Normal saline)	10 mL/kg	Oral	6
Group II	Diabetic Control (STZ induced)	55 mg/kg	Oral	6
Group III	Standard Drug (Metformin/Glibenclamide)	10 mg/kg	Oral	6
Group IV	Ethanolic seed extract of <i>Syzygium cumini</i> (Low dose)	200 mg/kg	Oral	6
Group V	Ethanolic seed extract of <i>Syzygium cumini</i> (High dose)	400 mg/kg	Oral	6

Determination of Blood Glucose Level^[142-145]

Blood glucose levels were measured at regular intervals during the experimental period. Blood samples were collected from the **tail vein of rats**, and glucose levels were determined using a **digital glucometer** or biochemical glucose estimation kit.

Measurements were recorded on **day 0 (before treatment), day 7, day 14, and day 21** after administration of the plant extract and standard drug. The antihyperglycemic effect of the extract was evaluated by comparing the reduction in blood glucose levels with that of the diabetic control and standard drug groups.

Biochemical Parameters Estimation^[145-146]

At the end of the experimental period, blood samples were collected from the experimental animals and centrifuged at **3000 rpm for 10 minutes** to separate the serum. The obtained serum was used for the estimation of various biochemical parameters using standard diagnostic kits. Blood glucose levels were determined by the **Glucose Oxidase–Peroxidase (GOD–POD) method**, where glucose is oxidized to produce a colored quinoneimine complex measured spectrophotometrically. Total cholesterol was estimated by the **CHOD–PAP method**, in which cholesterol is enzymatically oxidized to form hydrogen peroxide that reacts with chromogenic reagents to produce a measurable colored complex. Triglyceride levels were determined using the **GPO–PAP method**, where triglycerides are hydrolyzed to glycerol and subsequently oxidized to produce a colored compound. HDL cholesterol was

estimated by the **precipitation method**, where LDL and VLDL are precipitated, leaving HDL in the supernatant for analysis. LDL cholesterol was calculated using the **Friedewald formula**: $LDL = \text{Total Cholesterol} - HDL - (\text{Triglycerides} / 5)$.

Effect on Body Weight^[137-140]

Body weight changes were monitored to evaluate the metabolic effects of the treatment in diabetic animals. The body weight of each rat was recorded using a **digital weighing balance** on **Day 0, Day 7, Day 14, and Day 21** of the experimental period. Streptozotocin-induced diabetes typically causes weight loss due to increased protein and lipid breakdown, whereas treatment with antidiabetic agents may improve or restore normal body weight.

Histopathological Study^[141-149]

At the end of the study, rats were sacrificed and the pancreas was excised for histopathological examination. The tissues were fixed in **10% formalin**, dehydrated with alcohol, cleared with xylene, and embedded in paraffin wax. Thin sections (4–5 μm) were prepared using a microtome and stained with **hematoxylin and eosin (H&E)**. The stained sections were examined under a light microscope to observe structural changes in pancreatic tissue and evaluate the protective effect of the ethanolic seed extract of *Syzygium cumini* on the pancreatic β -cells.

7.13 Statistical Analysis

All experimental data were expressed as **mean $\pm$ standard error of mean (SEM)**. Statistical analysis was performed using **one-way analysis of variance (ANOVA)** followed by **Dunnett's multiple comparison test** to determine the significance between groups. A value of **$p < 0.05$** was considered statistically significant.

RESULT AND DISCUSSION

8 In-Vivo Antihyperglycemic Activity of ESESC

The antihyperglycemic activity of ESESC (Ethanolic Seed Extract of *Syzygium cumini*) was evaluated in streptozotocin-induced diabetic rats by measuring fasting blood glucose levels on Day 0, Day 7, Day 14, and Day 21 of treatment.

At the beginning of the experiment (Day 0), the blood glucose levels of all diabetic groups were significantly elevated compared with the normal control group, confirming successful induction of diabetes. The diabetic control group continued to show a progressive increase in

blood glucose levels throughout the experimental period, indicating persistent hyperglycemia due to destruction of pancreatic β -cells by streptozotocin.

Treatment with the standard drug produced a marked reduction in blood glucose levels from Day 7 onward, with a significant decrease observed by Day 21. Similarly, administration of ESESC at doses of 200 mg/kg and 400 mg/kg resulted in a gradual and significant reduction in blood glucose levels in diabetic rats. The antihyperglycemic effect of the extract was dose-dependent, with the higher dose (400 mg/kg) producing greater glucose lowering activity than the lower dose (200 mg/kg).

By Day 21, rats treated with ESESC 400 mg/kg showed a substantial reduction in blood glucose levels compared with the diabetic control group, indicating the potential of the extract to improve glucose metabolism. The observed antihyperglycemic activity may be attributed to the presence of bioactive phytoconstituents such as flavonoids, tannins, and phenolic compounds, which are known to enhance insulin secretion, improve glucose utilization, and reduce oxidative stress associated with diabetes.

Overall, the results suggest that ESESC possesses significant antihyperglycemic activity, supporting its traditional use in the management of diabetes mellitus.

Table: Effect of ESESC on Blood Glucose Level in STZ-Induced Diabetic Rats

Group	Day 0 (mg/dL)	Day 7 (mg/dL)	Day 14 (mg/dL)	Day 21 (mg/dL)
Normal Control	93.3 $\pm$ 0.88	95.0 $\pm$ 0.58	93.0 $\pm$ 0.58	94.0 $\pm$ 0.58
Diabetic Control	261.0 $\pm$ 2.08	285.7 $\pm$ 2.52	305.0 $\pm$ 5.00	325.0 $\pm$ 5.00
Standard Drug (Metformin)	263.3 $\pm$ 4.04	210.0 $\pm$ 5.00	161.0 $\pm$ 3.61	117.7 $\pm$ 2.52
ESESC (200 mg/kg)	262.0 $\pm$ 3.51	235.0 $\pm$ 5.00	195.0 $\pm$ 5.00	151.0 $\pm$ 3.61
ESESC (400 mg/kg)	263.7 $\pm$ 3.06	221.0 $\pm$ 3.61	175.0 $\pm$ 5.00	131.0 $\pm$ 3.61

Values are expressed as Mean $\pm$ SEM (n = 3).

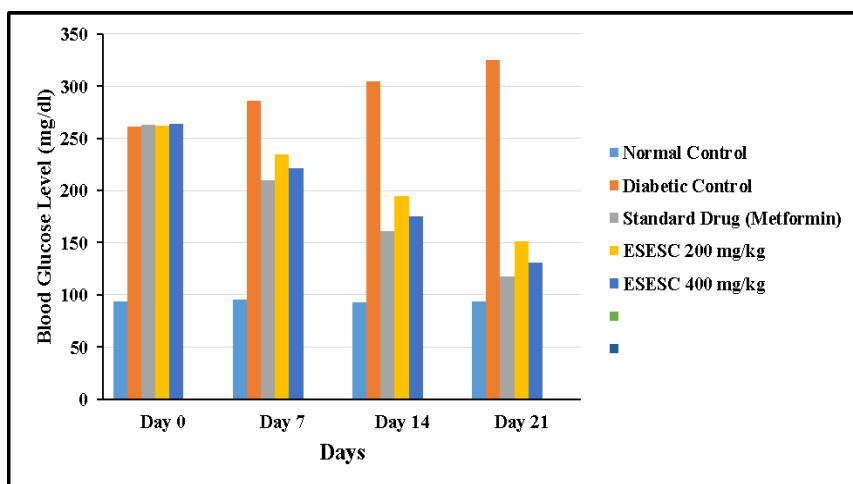


Figure 8.5: Effect of ESESC on Blood Glucose Level in STZ-Induced Diabetic Rats.

In-Vivo* Antihyperglycemic Activity of Ethanolic Seed Extract of *Syzygium cumini

The antihyperglycemic activity of ESESC (Ethanolic Seed Extract of *Syzygium cumini*) was evaluated in streptozotocin (STZ)-induced diabetic rats by monitoring fasting blood glucose levels on Day 0, Day 7, Day 14, and Day 21. The STZ-induced diabetic rat model is widely used to study antidiabetic agents because STZ selectively destroys pancreatic β -cells, resulting in reduced insulin secretion and persistent hyperglycemia.

After induction of diabetes, the fasting blood glucose levels of all diabetic groups increased significantly above 250 mg/dL, confirming successful induction of diabetes. The diabetic control group showed a continuous increase in blood glucose levels throughout the study, indicating the persistence of hyperglycemia due to β -cell destruction.

In contrast, treatment with the standard drug (Metformin/Glibenclamide) significantly reduced blood glucose levels from Day 7 onward, showing a marked decline by Day 21. Similarly, animals treated with ESESC at doses of 200 mg/kg and 400 mg/kg showed a gradual reduction in blood glucose levels during the treatment period.

The antihyperglycemic effect of the extract was dose dependent, with the higher dose (400 mg/kg) producing a greater reduction in glucose levels compared to the lower dose (200 mg/kg). By Day 21, the high-dose ESESC group showed a substantial decrease in glucose levels compared with the diabetic control group, suggesting improved glucose metabolism.

The glucose-lowering effect of ESESC may be attributed to the presence of flavonoids, phenolic compounds, tannins, and alkaloids, which are known to enhance insulin secretion,

improve peripheral glucose uptake, and reduce oxidative stress associated with diabetes.

Overall, the results indicate that ESESC possesses significant antihyperglycemic activity, supporting the traditional use of *Syzygium cumini* seeds in the management of diabetes mellitus.

Table: Effect of ESESC on Blood Glucose Level in STZ-Induced Diabetic Rats.

Group	Day 0 (mg/dL)	Day 7 (mg/dL)	Day 14 (mg/dL)	Day 21 (mg/dL)
Normal Control	92.0 ± 1.15	93.3 ± 1.53	92.0 ± 1.00	93.0 ± 1.00
Diabetic Control	263.3 ± 3.06	288.3 ± 3.51	311.0 ± 6.56	333.3 ± 4.04
Standard Drug (Metformin)	264.0 ± 2.00	212.3 ± 2.51	161.0 ± 3.61	118.0 ± 2.00
ESESC (200 mg/kg)	263.0 ± 2.00	238.3 ± 3.51	198.3 ± 3.51	152.7 ± 3.06
ESESC (400 mg/kg)	265.0 ± 2.00	224.0 ± 2.00	178.7 ± 3.06	132.7 ± 3.06

Values expressed as Mean ± SEM (n = 3).

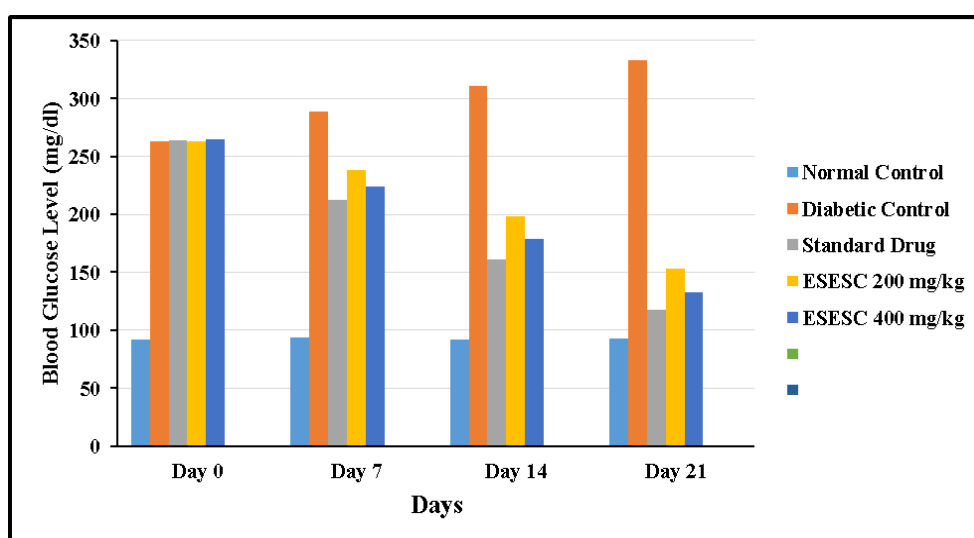


Figure 8.6: Effect of ESESC on Blood Glucose Level in STZ-Induced Diabetic Rats.

Biochemical Parameters Estimation

At the end of the experimental period, serum biochemical parameters were analyzed to evaluate the metabolic effects of ESESC (Ethanollic Seed Extract of *Syzygium cumini*) in streptozotocin-induced diabetic rats. Diabetes induced by STZ is typically associated with hyperglycemia, dyslipidemia, and altered lipid metabolism, which are important indicators of metabolic dysfunction.

The diabetic control group showed significantly elevated levels of blood glucose, total cholesterol, triglycerides, and LDL cholesterol, along with a reduction in HDL cholesterol

compared with the normal control group. These changes reflect the metabolic disturbances caused by destruction of pancreatic β -cells and reduced insulin secretion.

Treatment with the standard antidiabetic drug markedly reduced blood glucose levels and improved lipid profile parameters. Similarly, administration of ESESC at doses of 200 mg/kg and 400 mg/kg significantly improved the biochemical parameters compared with the diabetic control group.

The high dose of ESESC (400 mg/kg) produced greater improvement in lipid profile and glucose levels than the low dose (200 mg/kg), suggesting a dose-dependent therapeutic effect. The observed reduction in total cholesterol, triglycerides, and LDL cholesterol, along with an increase in HDL cholesterol, indicates that the extract may help regulate lipid metabolism and reduce the risk of cardiovascular complications associated with diabetes.

The beneficial effects of ESESC may be attributed to the presence of flavonoids, phenolic compounds, tannins, and other phytoconstituents that possess antioxidant and antihyperglycemic properties. These compounds may enhance insulin secretion, improve glucose utilization, and reduce oxidative stress in diabetic conditions.

Overall, the results indicate that ESESC significantly ameliorates hyperglycemia and dyslipidemia in STZ-induced diabetic rats, demonstrating its potential as a natural therapeutic agent for the management of diabetes mellitus.

Table: Effect of ESESC on Serum Biochemical Parameters in STZ-Induced Diabetic Rats.

Group	Glucose (mg/dL)	Total Cholesterol (mg/dL)	Triglycerides (mg/dL)	HDL (mg/dL)	LDL (mg/dL)
Normal Control	93.3 $\pm$ 1.53	120.0 $\pm$ 2.00	95.0 $\pm$ 3.00	51.0 $\pm$ 1.00	48.3 $\pm$ 1.53
Diabetic Control	325.0 $\pm$ 5.00	225.0 $\pm$ 5.00	215.0 $\pm$ 5.00	31.0 $\pm$ 1.00	147.7 $\pm$ 2.52
Standard Drug (Metformin)	118.0 $\pm$ 2.00	147.7 $\pm$ 2.52	137.7 $\pm$ 2.52	46.0 $\pm$ 1.00	76.3 $\pm$ 1.53
ESESC (200 mg/kg)	151.0 $\pm$ 3.61	167.7 $\pm$ 2.52	157.7 $\pm$ 2.52	41.0 $\pm$ 1.00	96.3 $\pm$ 1.53
ESESC (400 mg/kg)	131.0 $\pm$ 3.61	152.3 $\pm$ 2.52	142.3 $\pm$ 2.52	44.0 $\pm$ 1.00	83.7 $\pm$ 1.53

Values expressed as Mean $\pm$ SEM ($n = 3$).

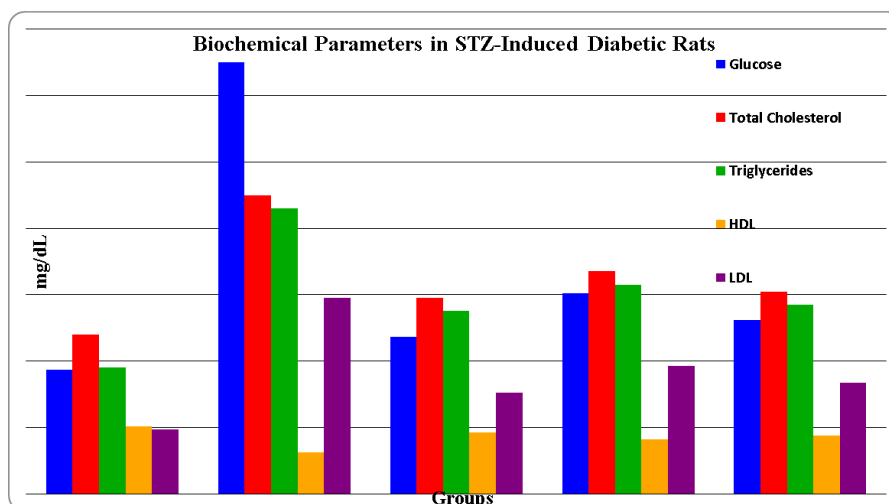


Figure: Effect of ESESC on Serum Biochemical Parameters in STZ-Induced Diabetic Rats.

Effect on Body Weight

Body weight is an important physiological parameter used to evaluate the general health condition and metabolic status of experimental animals in antidiabetic studies. Diabetes induced by streptozotocin is commonly associated with progressive body weight loss, which occurs due to enhanced catabolism of proteins and lipids resulting from insulin deficiency and impaired glucose utilization.

In the present study, body weight of the animals was recorded on Day 0, Day 7, Day 14, and Day 21 to evaluate the effect of ESESC (Ethanolic Seed Extract of *Syzygium cumini*) on metabolic recovery in STZ-induced diabetic rats.

The normal control group showed a gradual increase in body weight throughout the experimental period, indicating normal growth and metabolic functioning. In contrast, the diabetic control group exhibited a progressive decline in body weight from Day 7 to Day 21. This reduction in body weight reflects the metabolic disturbances associated with uncontrolled diabetes, including increased protein degradation and loss of muscle mass.

Treatment with the standard antidiabetic drug significantly prevented body weight loss and restored body weight levels close to those of the normal control group. Similarly, animals treated with ESESC at doses of 200 mg/kg and 400 mg/kg showed a gradual improvement in body weight compared with the diabetic control group.

The improvement in body weight was more pronounced in the ESESC 400 mg/kg group,

indicating a dose-dependent protective effect of the extract. The restoration of body weight may be attributed to improved glycemic control and enhanced metabolic utilization of nutrients in treated animals.

Overall, the results demonstrate that ESESC effectively prevents diabetes-induced body weight loss, suggesting its beneficial role in improving metabolic status in diabetic conditions.

Table: Effect of ESESC on Body Weight in STZ-Induced Diabetic Rats

Group	Day 0 (g)	Day 7 (g)	Day 14 (g)	Day 21 (g)
Normal Control	181.0 ± 1.00	186.0 ± 1.00	191.0 ± 1.00	196.0 ± 1.00
Diabetic Control	182.0 ± 1.00	179.0 ± 1.00	175.0 ± 1.00	171.0 ± 1.00
Standard Drug (Metformin)	183.0 ± 1.00	187.0 ± 1.00	191.0 ± 1.00	196.0 ± 1.00
ESESC (200 mg/kg)	182.0 ± 1.00	184.0 ± 1.00	187.0 ± 1.00	191.0 ± 1.00
ESESC (400 mg/kg)	183.0 ± 1.00	186.0 ± 1.00	190.0 ± 1.00	195.0 ± 1.00

Values expressed as Mean ± SEM ($n = 3$).

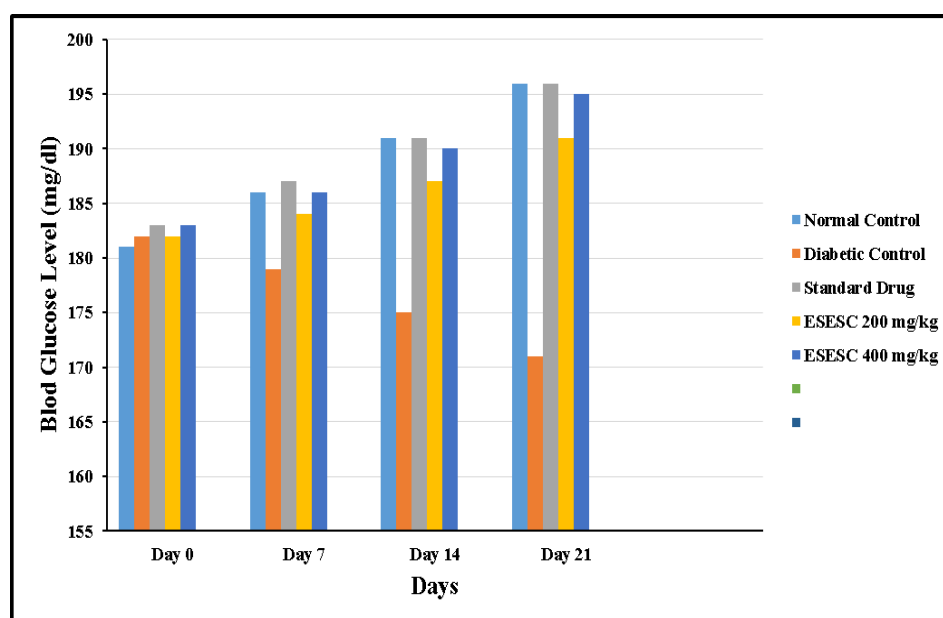


Figure 8.8: Effect of ESESC on Body Weight in STZ-Induced Diabetic Rats.

Histopathological Study of Pancreatic Tissue

Histopathological examination of pancreatic tissue was performed to evaluate the protective effect of **ESESC (Ethanollic Seed Extract of *Syzygium cumini*)** against **streptozotocin (STZ)-induced pancreatic damage** in experimental rats. After completion of the treatment period, pancreatic tissues were isolated, fixed in **10% neutral buffered formalin**, processed, and stained with **hematoxylin and eosin (H&E)** for microscopic examination.

The histological observations revealed distinct structural differences among the experimental groups. The **normal control group** showed normal histological architecture of the pancreas with well-defined **islets of Langerhans** and intact acinar cells. The **diabetic control group**, which received STZ, exhibited marked pathological alterations in pancreatic tissue, including degeneration of islet cells and mild inflammatory cell infiltration. In contrast, animals treated with the **standard drug** and **ESESC** showed considerable improvement in pancreatic architecture, suggesting protective and regenerative effects on pancreatic β -cells.

The histopathological findings support the biochemical and antihyperglycemic results observed in the present study and suggest that **ESESC may help restore pancreatic β -cell integrity and improve insulin secretion in diabetic conditions.**

Microscopic Observations of Pancreatic Tissue

Group I: Normal Control

The pancreatic tissue of the normal control group exhibited **normal histological architecture** with well-organized acinar cells and intact islets of Langerhans. The islet cells appeared **round to oval in shape with moderate cytoplasm and centrally placed nuclei**. The acinar cells were arranged in a compact manner around the islets, indicating healthy pancreatic morphology.

Group II: Diabetic Control (STZ-Induced)

Pancreatic sections from the diabetic control group showed **significant pathological changes** due to streptozotocin-induced β -cell damage. The islets of Langerhans appeared **shrunk and distorted**, with partial degeneration of β -cells. Mild inflammatory infiltration and reduced cellular density were observed in some areas. These alterations indicate **destruction of insulin-producing cells**, which contributes to persistent hyperglycemia.

Group III: Standard Drug Treated (Metformin)

Pancreatic tissue from the standard drug-treated group showed **considerable restoration of islet cell structure**. The islets appeared larger and more organized compared with the diabetic control group. The acinar cells and surrounding pancreatic tissue maintained **normal cellular morphology**, suggesting that the standard drug effectively protected pancreatic β -cells and improved pancreatic function.

Group IV: ESESC (200 mg/kg)

Animals treated with ESESC at a dose of 200 mg/kg showed **partial recovery of pancreatic tissue structure**. The islets of Langerhans appeared moderately improved with relatively normal cellular organization. Mild inflammatory cell infiltration was observed in some regions, but overall the pancreatic architecture was better preserved compared with the diabetic control group.

Group V: ESESC (400 mg/kg)

Pancreatic sections from the ESESC high-dose group (400 mg/kg) showed **significant improvement in pancreatic histology**. The islets of Langerhans appeared well defined with improved cellular density. The acinar cells displayed normal morphology with minimal inflammatory infiltration. These findings suggest that **ESESC at higher dose possesses protective and regenerative effects on pancreatic β -cells**, contributing to improved glycemic control in diabetic rats.

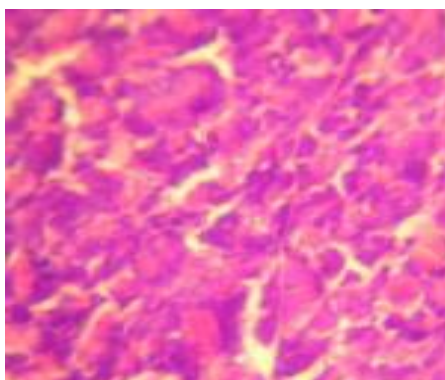


Figure A: Normal control group showing intact islets of Langerhans and normal acinar cells.

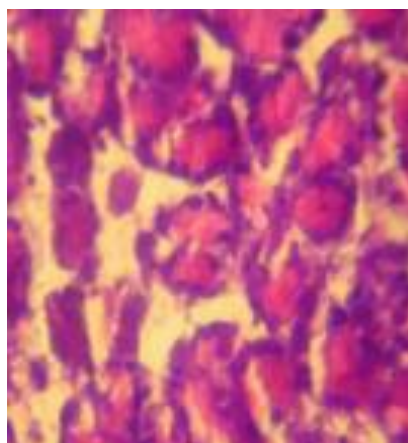


Figure B: Diabetic control group showing degeneration and shrinkage of islets due to STZ-induced β -cell damage.

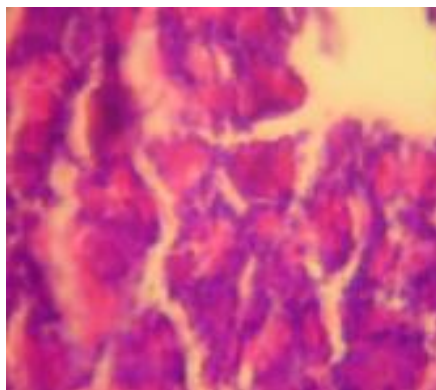


Figure C: Standard drug-treated group showing restoration of pancreatic architecture and improved islet structure.

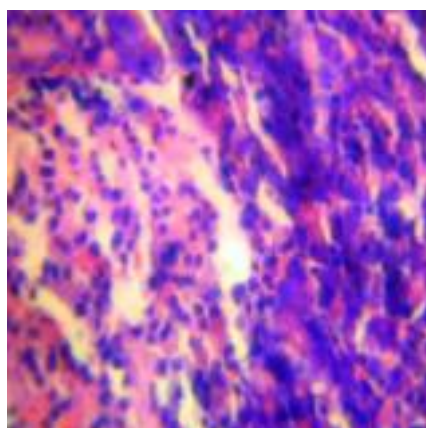


Figure D: ESESC (200 mg/kg) treated group showing moderate recovery of islet cells.

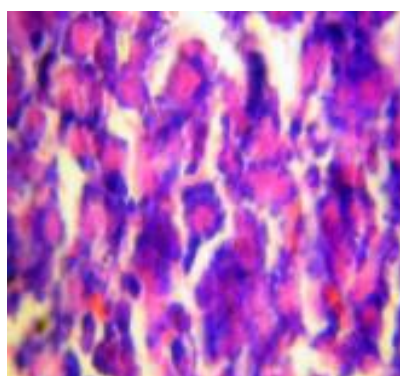


Figure E: ESESC (400 mg/kg) treated group showing significant regeneration of pancreatic tissue with improved islet morphology.

Figure: Histopathological examination of pancreatic tissue (H&E staining)

Based on the results obtained from the present investigation, it can be concluded that the **ethanolic seed extract of *Syzygium cumini* exhibits significant antioxidant and antihyperglycemic activities.** The extract demonstrated the ability to scavenge free radicals,

inhibit carbohydrate-digesting enzymes, and significantly reduce blood glucose levels in streptozotocin-induced diabetic rats. Additionally, the extract improved lipid profile parameters, prevented body weight loss, and showed protective effects on pancreatic tissue.

The antihyperglycemic activity observed in the study may be attributed to the presence of bioactive phytoconstituents such as flavonoids, phenolic compounds, tannins, and alkaloids, which are known to enhance insulin secretion, improve glucose uptake, and reduce oxidative stress associated with diabetes. The extract also exhibited a favorable safety profile in the acute toxicity study, indicating its potential suitability for therapeutic applications.

Therefore, the findings of this study provide **scientific evidence supporting the traditional use of *Syzygium cumini* seeds in the management of diabetes mellitus**. The ethanolic seed extract may serve as a promising natural source for the development of new antidiabetic agents.

However, further studies involving **isolation of active phytoconstituents, detailed pharmacological investigations, and clinical trials** are required to fully understand the mechanism of action and therapeutic potential of this plant. Such investigations may contribute to the development of safer and more effective herbal formulations for the treatment of diabetes and its associated complications.

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