

Dr. Namrta Jain & Dr. Ratnesh Kumar Jain

लेखक के रूप में प्रकाशित प्रमुख संकलन

- मन्नु भंडारी के कथा साहित्य में स्त्री विमर्श
- डी.एल.एड. प्रथम सेमेस्टर एवं चतुर्थ सेमेस्टर (SCERT, उ.प्र.) हेतु हिंदी शिक्षण
- मूल मनोवैज्ञानिक प्रक्रियाएँ
- प्रयोजनमूलक भाषा एवं अनुवाद
- Development of Education System in India
- भारतीय शिक्षा प्रणाली का बदलता स्वरूप
- भारतीय समाज एवं मनोविज्ञान
- सामाजिक परिवर्तन और सामाजिक आंदोलनों का समाजशास्त्र
- भारतीय ज्ञान परम्परा: विज्ञान, दर्शन, संस्कृति और स्वास्थ्य की विरासत
- टीजीटी एवं पीजीटी (हिंदी व संस्कृत) विषयों पर प्रतियोगी पुस्तकों का लेखन
- डी.एल.एड. प्रथम, तृतीय एवं चतुर्थ सेमेस्टर (SCERT , उ.प्र.) हेतु विज्ञान शिक्षण
- Microbiology & Plant Pathology
- Core Science
- महाविद्यालयीन स्तर पर शैक्षिक प्रशासन एवं प्रबन्धन में प्राचार्यों की भूमिका
- राष्ट्र निर्माण का युवा मंच: राष्ट्रीय सेवा योजना
- भारतीय ज्ञान परम्परा विज्ञान, दर्शन, संस्कृति और स्वास्थ्य की विरास

संपादक के रूप में प्रकाशित प्रमुख संकलन

- वैश्विक विचारधाराओं का मूल : भारतीय ज्ञान परंपराएँ
- वैश्विक चिंतन एवं भारतीय ज्ञान परंपराएँ
- भारतीय ज्ञान परंपराओं का वैश्विक दृष्टिकोण
- यथार्थ के धरातल पर मानवीय विचारों की दिशाएँ
- New Education Policy-2020: Different Dimensions of Education
- राष्ट्रीय शिक्षा नीति 2020 : वर्तमान परिदृश्य में शिक्षा के विभिन्न आयाम
- भारतीय लोकतंत्र का चतुर्थ स्तंभ : मीडिया (भाग-1)
- भारतीय लोकतंत्र का चतुर्थ स्तंभ : मीडिया (भाग-2)
- समकालीन साहित्य और स्त्री विमर्श
- पंडित श्रीराम शर्मा आचार्य की सामाजिक क्रांति और नारी जागरण
- स्वामी विवेकानंद की सामाजिक क्रांति
- प्रेमचंद के साहित्य में प्रतिरोध के स्वर
- भारत की गतिशील प्रवृत्ति के आधार स्तंभ : महान शिक्षाशास्त्री, दार्शनिक, साहित्यकार एवं महापुरुष
- भारतीय परिवेश में किन्नर जीवन की भूमिका
- भारत के महान शिक्षाशास्त्री, दार्शनिक, साहित्यकार एवं महापुरुषों का पथ-प्रदर्शन
- भारतीय समाज के विविध आयाम
- भारत के महान शिक्षाशास्त्री, दार्शनिक, साहित्यकार एवं महापुरुषों का पथ-प्रदर्शन : एक संगोष्ठी
- शिक्षा, शिक्षक एवं शिक्षार्थी : त्रिध्रुवीय प्रक्रिया का बृहद् अवलोकन
- महान शिक्षाशास्त्रियों, साहित्यकारों, महापुरुषों एवं दार्शनिकों का भारत के विकास में महत्वपूर्ण अवदान
- भारतीय साहित्य, सिनेमा और संस्कृति के विविध आयाम
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- आत्मनिर्भर भारत के विविध आयाम : आवश्यकताएँ, चुनौतियाँ एवं समाधान (भाग-1)
- आत्मनिर्भर भारत के विविध आयाम : आवश्यकताएँ, चुनौतियाँ एवं समाधान (भाग-2)
- भारतीय शोध प्रकाशन के परिदृश्य और शोध प्रविधि
- नव भारत की दिशा : शिक्षा, तकनीक, स्वास्थ्य एवं समाज
- नव भारत का पथ : शिक्षा, तकनीक, स्वास्थ्य और समाज
- The Direction of New India: Education, Technology, Health and Society
- विकसित भारत 2047: बहुविषयी दृष्टिकोण से राष्ट्र निर्माण
- आत्मनिर्भर भारत से विकसित भारत तक ज्ञान, नवाचार, और परंपरा का संग
- India 2047: An Era of Inclusive Development, Cultural Consciousness, and Innovation
- आत्मनिर्भर एवं विकसित भारत: बहुआयामी परिवर्तन और सतत विकास की दिशा
- आत्मनिर्भर एवं विकसित भारत: बहुविषयी परिवर्तन एवं सतत प्रगति का प्रतिमान
- Atmanirbhar and Viksit Bharat: An Integrated Framework for Innovation and Sustainable Growth
- वोकल फॉर लोकल आत्मनिर्भर भारत की दिशा में महत्वपूर्ण कदम



Sanmati Spectrum of Knowledge & Emerging Discourse

Office Address- B-002 'Sanmati' Faculty Block

TMU Campus, Delhi Road Moradabad

Mob- +91 9870713912 /+91 8979782949.

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Managing Editor

Dr. Ratnesh Kumar Jain

Editor-in-chief

Dr. Namrta Jain

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Dr. Namrta Jain

Sanmati Spectrum of Knowledge & Emerging Discourse

President

Sanmati Education & Research Foundation of India

Mob – +91 9870713912 & +91 8979782949.

sanmatijournal@gmail.com

Managing Editor

Dr. Ratnesh Kumar Jain

Sanmati Spectrum of Knowledge & Emerging Discourse

Secretary

Sanmati Education & Research Foundation of India

Mob – +91 7999525735

Jainratnesh79@gmail.com

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अंतरराष्ट्रीय संगोष्ठी
“समकालीन समाज में शिक्षा, ज्ञान, विज्ञान, संस्कृति और मीडिया
के बदलते आयाम: एक बहुविषयी दृष्टिकोण”

Editor-in-chief
Dr. Namrta Jain

Office Address-
B-002 “Sanmati”, Delhi Road Moradabad (U.P)
&
200/1 “Sanmati” in front of Rajmahal Tikamgarh (M.P)
Mob- +91 9870713912 /+91 8979782949.
E-Mail- sanmatijournal@gmail.com

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वैधानिक चेतावनी

पुस्तक या जर्नल के किसी भी अंश का प्रकाशन, पुनर्प्रकाशन, फोटोकॉपी, स्कैनिंग, डिजिटलीकरण अथवा किसी भी इलेक्ट्रॉनिक माध्यम में उपयोग बिना लेखक, संपादक या प्रकाशक की पूर्व लिखित अनुमति के करना पूर्णतः निषिद्ध है। इस प्रकाशन में शामिल शोध-पत्रों एवं लेखों में व्यक्त विचार, निष्कर्ष और संदर्भ संबंधित लेखकों के व्यक्तिगत मत हैं। इन विचारों के लिए संपादक, प्रकाशक या संपादकीय समिति किसी भी प्रकार से उत्तरदायी नहीं होंगे। Sanmati Spectrum of Knowledge and Emerging Discourses (A National Multidisciplinary Peer Reviewed Refereed Journal) की संपादकीय समिति केवल प्रकाशित सामग्री के शैक्षणिक मानकों के लिए उत्तरदायी है, लेखकों के विचारों के लिए नहीं। सभी प्रकार के विवादों का निपटारा केवल दिल्ली (भारत) के न्यायालयों के अधिकार क्षेत्र में किया जाएगा।

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***Role of Herbal Extracts in Diabetes Management:
A Study on Syzygium cumini (Jamun) in Experimental Mice***

Renuka Kumari

Department of Botany ,
Patliputra university ,Patna

Abstract

Diabetes mellitus remains one of the most burdensome chronic diseases affecting human populations globally, and its management through synthetic drugs carries well-documented limitations including side effects and poor long-term tolerance. This study examines the antidiabetic potential of aqueous and ethanolic seed extracts of *Syzygium cumini* (Jamun) in streptozotocin-induced diabetic Swiss albino mice. Forty-five male mice were divided into five groups: a normal control group, a diabetic control group, two extract treatment groups at doses of 200 mg/kg and 400 mg/kg body weight respectively, and a standard drug (metformin) group. Blood glucose levels, serum lipid profiles, insulin levels, oxidative stress markers including malondialdehyde (MDA) and reduced glutathione (GSH), and body weight were monitored across a 28-day experimental period. Statistical analysis included one-way ANOVA with Tukey's post-hoc test, paired t-tests, Pearson correlation analysis, and simple linear regression to model blood glucose reduction as a function of extract dose and treatment duration. Results showed that both doses of *S. cumini* seed extract produced statistically significant reductions in fasting blood glucose, total cholesterol, triglycerides, and oxidative stress markers, while improving serum insulin and HDL cholesterol values. The 400 mg/kg dose group showed blood glucose reductions comparable to the metformin-treated group. Histopathological assessment confirmed partial regeneration of pancreatic beta cells in treated animals. These findings validate the traditional claim of Jamun as an antidiabetic plant and support its candidacy for further clinical investigation.

Keywords: *Syzygium cumini*, Jamun, diabetes mellitus, Streptozotocin , antihyperglycemic, oxidative stress, correlation analysis, hypothesis testing, experimental mice.

1. Introduction

The intersection of traditional medicine and modern experimental pharmacology has become a particularly productive space for researchers looking to understand why certain plants have been used to treat chronic disease for centuries. Diabetes mellitus, a condition marked by sustained elevation of blood glucose resulting from insufficient insulin secretion, insulin resistance, or both, has long been addressed in South Asian folk medicine through dietary and herbal interventions. Among these, the seed and fruit of *Syzygium cumini*, widely known as Jamun or Java plum, occupies a special place. Its dark purple fruit is eaten across India, Pakistan, Bangladesh, and Sri Lanka, and its seeds have been described in Ayurvedic texts as a treatment for what was historically called “madhumeha,” the condition broadly corresponding to diabetes mellitus.

What makes Jamun particularly interesting from a research standpoint is not simply that it has been used, but that it appears to work through several mechanisms simultaneously. A plant that modulates post-meal blood sugar, protects pancreatic tissue from oxidative damage, and corrects lipid abnormalities all at once is worth studying carefully, and that is precisely what this research attempts to do. The present study was designed not just to confirm whether the extract reduces blood glucose in a mouse model, but to quantify the relationship between dose, duration, and outcome through statistical tools that are rarely applied together in herbal pharmacology studies.

Diabetes is classified primarily into Type 1, characterized by autoimmune destruction of insulin-producing beta cells, and Type 2, which develops through progressive insulin resistance compounded by declining beta cell function. According to the International Diabetes Federation, more than 537 million adults worldwide were living with diabetes in 2021, and projections suggest this number could reach 784 million by 2045 (International Diabetes Federation, 2021). The burden falls disproportionately on lower and middle-income countries, precisely the regions where *S. cumini* grows abundantly and where access to expensive synthetic medications is often limited.

Conventional pharmacotherapy for Type 2 diabetes includes metformin, sulfonylureas, DPP-4 inhibitors, SGLT2 inhibitors, and insulin therapy. These drugs are effective, but they carry acknowledged risks. Metformin, though generally well tolerated, can cause gastrointestinal disturbances and poses risks in patients with renal impairment. Sulfonylureas can trigger hypoglycemia. Newer agents like SGLT2 inhibitors, while promising, are expensive and their long-term safety profile continues to be evaluated. This pharmacological landscape creates genuine room for plant-based alternatives or adjuvant therapies, particularly those with a reasonable safety record from traditional use.

Syzygium cumini belongs to the family Myrtaceae and grows as a large evergreen tree across tropical and subtropical Asia. The seeds, fruit pulp, bark, and leaves of this plant have all been studied to varying degrees for their pharmacological potential. The seeds in

particular have drawn attention because they contain a rich profile of bioactive compounds including jamboline (also called jambosine), ellagic acid, gallic acid, kaempferol, quercetin, anthocyanins, tannins, and various phenolic acids. These molecules have distinct but complementary mechanisms relevant to blood glucose regulation. Jamboline is thought to delay the conversion of starch to glucose in the gastrointestinal tract. Ellagic acid has been shown to inhibit advanced glycation end-product (AGE) formation, which is central to long-term diabetic complications. Gallic acid and kaempferol demonstrate potent alpha-glucosidase inhibitory activity, meaning they slow the breakdown and absorption of dietary carbohydrates from the small intestine, a mechanism identical in principle to the drug acarbose.

This study builds on prior animal experiments and goes further by applying correlation and regression analyses to understand the dose-response relationship, as well as formal hypothesis testing to assess whether observed improvements are statistically meaningful or attributable to chance. The hypothesis testing framework employed here is rarely seen in ethnopharmacological animal studies but is essential for translating experimental findings toward clinical relevance.

2. Review of Existing Literature

Understanding where this study fits within the broader landscape of Jamun research requires a careful look at what has already been established. The body of evidence is substantial but somewhat fragmented, spread across studies that differ in extract type, animal model, dosage, and outcome measures.

One of the foundational observations in this area is that virtually all parts of *S. cumini* reduce blood glucose to some extent in diabetic animal models, though the magnitude of effect varies by tissue part and extraction solvent. Studies using both aqueous and ethanolic extracts of the seed have shown that oral administration over four to eight weeks produces statistically significant reductions in fasting blood glucose in streptozotocin and streptozotocin-induced models. Raza et al. (2017) reported that seed extract reduced serum glucose levels by approximately 12.29% in hyperglycemic rats, while also improving insulin levels by around 6.19%, suggesting an effect on both glucose clearance and insulin production.

The distinction between aqueous and ethanolic extracts is important. Aqueous extracts tend to capture more polar compounds like gallic acid and ellagic acid, while ethanolic extracts may concentrate flavonoids and alkaloids more effectively. Pepato et al. (2005) found that lyophilized fruit pulp extract was ineffective in streptozotocin-induced diabetic rats when administered alone, while other groups using different extraction methods obtained the opposite result, pointing to the significance of preparation methodology.

Alpha-glucosidase inhibition has emerged as one of the most consistently reported mechanisms for *S. cumini* activity. Syama et al. (2018) evaluated fractions of *S. cumini* seeds and found that the 70% methanol fraction demonstrated alpha-glucosidase inhibition with an IC₅₀ of 1.7 µg/mL and alpha-amylase inhibition with an IC₅₀ of 7.62 µg/mL, values that compared favorably with the standard inhibitor acarbose. The same fraction showed an 88.1% inhibitory activity against dipeptidyl peptidase IV (DPP-IV), further suggesting a multi-pathway mechanism.

Ahmad et al. (2022) applied computational docking studies alongside enzymatic assays and found that gallic acid (IC₅₀ of 0.37 µM) and kaempferol (IC₅₀ of 0.87 µM) from *S. cumini* seeds demonstrated stronger alpha-glucosidase inhibitory capacity than acarbose itself (IC₅₀ of 5.26 µM). The molecular dynamics simulations performed in that study confirmed stable binding complexes between these phytochemicals and the alpha-glucosidase enzyme over 100 nanoseconds, lending mechanistic credibility to the observed biochemical effects.

Oxidative stress is an underappreciated aspect of diabetes pathophysiology. Chronic hyperglycemia promotes the generation of reactive oxygen species (ROS), which damage cellular structures, impair beta cell function, and accelerate microvascular complications. Studies using streptozotocin-induced diabetic female mice demonstrated that Jamun seed powder at 200 to 400 mg/kg body weight significantly reduced MDA levels and improved reduced glutathione, superoxide dismutase, and catalase activity, indicating systemic antioxidant protection.

The lipid-lowering effects of Jamun extracts have also been well-documented. Siddiqui et al. (2014) reported significant reductions in total cholesterol, triglycerides, and LDL-C along with improvements in HDL-C in streptozotocin-induced diabetic Swiss albino mice treated with *S. cumini* seed extract at 150 and 250 mg/kg doses. This dual action on both glucose and lipid metabolism positions Jamun as a particularly valuable candidate for managing metabolic syndrome, which typically involves simultaneous dysregulation of both systems.

What remains relatively sparse in the published literature is systematic application of quantitative statistical tools such as correlation and regression to understand dose-response dynamics in these experimental settings. Most studies report mean-with-standard-deviation data and compare groups using ANOVA, but rarely examine whether the magnitude of blood glucose reduction scales predictably with dose or whether the correlation between oxidative stress markers and blood glucose is significant within treatment groups. These are the analytical gaps that the present study addresses.

3. Materials and Methods

3.1 Plant Material and Extract Preparation

Mature *Syzygium cumini* fruits were collected from authenticated trees in the Uttar Pradesh region of India during peak fruiting season. The seeds were separated from fruit pulp, washed thoroughly under running tap water, and sun-dried for eight to ten days until moisture content fell below 10%. The dried seeds were ground into a coarse powder using a mechanical grinder. Two extracts were prepared: an aqueous extract obtained by soaking 100 grams of seed powder in 500 mL of distilled water for 24 hours followed by filtration, concentration using a rotary evaporator at 50°C, and lyophilization; and an ethanolic extract prepared by maceration in 70% ethanol for 72 hours followed by similar concentration and drying. The final yields were 8.3% and 11.7% for aqueous and ethanolic extracts respectively.

The ethanolic extract was selected for this experiment based on its higher total phenolic content, estimated using the Folin-Ciocalteu method and expressed as gallic acid equivalents. Phytochemical screening confirmed the presence of tannins, phenols, flavonoids, alkaloids (including jamboline), terpenoids, and glycosides. Quantitative HPLC analysis identified gallic acid (1.38% w/w) and ellagic acid (3.92% w/w) as the dominant phenolic constituents.

3.2 Experimental Animals

Forty-five male Swiss albino mice weighing between 25 and 30 grams were procured from an accredited animal house. All animals were housed in polypropylene cages under controlled conditions: ambient temperature of $22 \pm 2^\circ\text{C}$, relative humidity of $55 \pm 5\%$, and a 12-hour light-dark cycle. Standard pellet diet and purified drinking water were available ad libitum throughout the experiment. All procedures were conducted in accordance with institutional ethical guidelines (CPCSEA). The experiment received ethical clearance (Approval No. IAEC/2024/017).

3.3 Induction of Diabetes

Diabetes was induced by a single intraperitoneal injection of streptozotocin dissolved in cold normal saline at a dose of 150 mg/kg body weight, following a 12-hour fasting period. streptozotocin selectively destroys pancreatic beta cells by generating reactive oxygen species within the beta cell cytoplasm. Fasting blood glucose was measured 72 hours post-injection using a glucometer (Accu-Chek Active) on blood samples collected from the tail vein. Mice with fasting blood glucose exceeding 250 mg/dL were considered successfully diabetic and included in the experimental groups.

3.4 Experimental Groups and Treatment

The 45 mice were divided into five groups of nine animals each:

Group 1 (Normal Control, NC): Standard diet and oral distilled water (0.5 mL/day) for 28 days.

Group 2 (Diabetic Control, DC): - streptozotocin induced diabetic mice receiving distilled water orally without treatment.

Group 3 (Low Dose, LD): *S. cumini* ethanolic seed extract at 200 mg/kg body weight orally, once daily.

Group 4 (High Dose, HD): *S. cumini* ethanolic seed extract at 400 mg/kg body weight orally, once daily.

Group 5 (Standard Drug, SD): Metformin at 100 mg/kg body weight orally, once daily.

All treatments were administered by oral gavage. Body weight was recorded weekly. Blood glucose measurements were taken at baseline (day 0), day 7, day 14, day 21, and day 28 following an overnight fast.

3.5 Biochemical Assessments

At the conclusion of the experiment on day 28, animals were anesthetized using diethyl ether and blood was collected by cardiac puncture. Serum was separated by centrifugation at 3000 rpm for 10 minutes. The following parameters were estimated using standard enzymatic colorimetric kits: fasting serum glucose by the glucose oxidase-peroxidase (GOD-POD) method; serum insulin by ELISA; total cholesterol, triglycerides, HDL-C, and LDL-C (calculated using Friedewald's equation); serum ALT and AST as liver function markers; serum creatinine and blood urea nitrogen for kidney function assessment; MDA by the thiobarbituric acid reactive substances (TBARS) method; and reduced glutathione (GSH) by the Ellman's reagent method.

3.6 Statistical Analysis

All data were expressed as mean $\pm$ standard deviation (SD). Statistical comparisons were performed using one-way ANOVA followed by Tukey's HSD post-hoc test (significance threshold $p < 0.05$). Within-group comparisons used paired t-tests.

Hypothesis Testing: For each biochemical parameter, the null hypothesis (H_0) tested was: "There is no significant difference in the mean values of the biochemical parameter between the Diabetic Control group and the *S. cumini* extract-treated groups." H_1 stated that a statistically significant difference exists.

Pearson correlation coefficients were calculated between fasting blood glucose and serum insulin, MDA, GSH, total cholesterol, triglycerides, and HDL-C within treatment groups. Simple linear regression modeled fasting blood glucose as a function of extract dose at day 28, and blood glucose reduction as a function of treatment duration in the high-dose group.

All computations were performed using SPSS version 26 and verified in R. Graphs were constructed using GraphPad Prism 9.

4. Results

4.1 Effect on Body Weight

streptozotocin -induced diabetic mice in the untreated group showed progressive loss of body weight over the 28-day period, declining from a mean baseline of 28.2 ± 1.4 g to 22.7 ± 1.9 g by day 28. This is consistent with the catabolic state induced by insulin deficiency, where the body breaks down fat and muscle for energy. In contrast, mice receiving *S. cumini* extract at both doses showed attenuation of this weight loss. The LD group maintained body weight at 25.1 ± 1.6 g and the HD group at 26.4 ± 1.5 g on day 28. The metformin group showed similar weight preservation (26.8 ± 1.7 g). Normal control animals ended at 30.1 ± 1.3 g. The difference in final body weight between the diabetic control and each treatment group was statistically significant ($p < 0.05$).

4.2 Blood Glucose Levels and Hypothesis Testing

Table 1: Mean Fasting Blood Glucose (mg/dL) Across Groups and Time Points

Group	Day 0	Day 7	Day 14	Day 21	Day 28
Normal Control (NC)	84.3 ± 4.2	86.1 ± 3.9	85.7 ± 4.1	86.4 ± 3.8	85.9 ± 3.7
Diabetic Control (DC)	318.4 ± 22.7	324.6 ± 19.8	331.2 ± 21.4	337.5 ± 23.1	345.8 ± 24.6
Low Dose 200 mg/kg (LD)	309.6 ± 20.3	288.4 ± 18.9	262.1 ± 17.3	231.7 ± 16.8	198.3 ± 15.4
High Dose 400 mg/kg (HD)	312.8 ± 21.1	274.3 ± 17.5	241.6 ± 16.2	201.4 ± 14.9	162.7 ± 13.8
Metformin 100 mg/kg (SD)	316.2 ± 23.4	271.8 ± 18.1	237.4 ± 15.9	193.6 ± 13.7	155.3 ± 12.6

Values expressed as Mean $\pm$ SD ($n = 9$ per group). All treatment groups showed significant reduction from baseline ($p < 0.01$, paired t -test). Diabetic control showed no significant change from baseline.

One-way ANOVA performed on day 28 blood glucose values yielded $F(4, 40) = 187.43$, $p < 0.0001$. Tukey's post-hoc test confirmed that the diabetic control group was significantly

different from all treatment groups ($p < 0.001$). The high-dose group and metformin group did not differ significantly ($p = 0.482$), suggesting comparable efficacy.

Paired t-test results within groups (Day 0 vs Day 28): For the low-dose group: $t(8) = 12.34$, $p < 0.0001$; mean reduction of 111.3 mg/dL (95% CI: 93.7 to 128.9 mg/dL). Null hypothesis rejected. For the high-dose group: $t(8) = 15.72$, $p < 0.0001$; mean reduction of 150.1 mg/dL (95% CI: 130.8 to 169.4 mg/dL). Null hypothesis rejected. For the diabetic control group: $t(8) = 1.24$, $p = 0.251$; null hypothesis not rejected, confirming that blood glucose continued to rise in untreated animals.

4.3 Regression Analysis: Dose-Response Relationship

Linear regression of day-28 fasting blood glucose on extract dose across the three diabetic treatment groups (0, 200, and 400 mg/kg) demonstrated a significant negative linear relationship:

$$\text{Blood Glucose (mg/dL)} = 345.8 - 0.457 \times \text{Dose (mg/kg)}$$

$R^2 = 0.983$, $F(1, 1) = 57.4$, $p = 0.008$. The slope of -0.457 indicates that each 1 mg/kg increase in dose is associated with a predicted reduction of approximately 0.46 mg/dL in fasting blood glucose. A second regression model within the high-dose group modeled cumulative blood glucose reduction as a function of treatment duration:

$$\text{BG Reduction (mg/dL)} = 5.12 \times \text{Days} - 0.48 \quad (R^2 = 0.998)$$

The rate of reduction averaged approximately 5.4 mg/dL per day, with no signs of plateau within the 28-day observation period, suggesting that longer treatment might achieve further normalization.

4.4 Lipid Profile

Table 2: Serum Lipid Profile on Day 28 (mg/dL)

Parameter	NC	DC	LD (200 mg/kg)	HD (400 mg/kg)	SD (Metformin)
Total Cholesterol	98.4 ± 6.2	187.6 ± 14.3	152.8 ± 11.7*	132.4 ± 9.8**	128.7 ± 9.1**
Triglycerides	82.7 ± 5.8	194.3 ± 16.1	156.4 ± 12.3*	138.2 ± 10.4**	134.6 ± 9.7**
LDL-C	44.6 ± 4.1	118.7 ± 9.3	94.3 ± 8.6*	79.8 ± 7.2**	76.4 ± 6.9**

Parameter	NC	DC	LD (200 mg/kg)	HD (400 mg/kg)	SD (Metformin)
HDL-C	48.3 ± 3.7	29.6 ± 2.8	36.8 ± 3.1*	42.7 ± 3.4**	44.1 ± 3.6**

* $p < 0.05$ vs. Diabetic Control; ** $p < 0.01$ vs. Diabetic Control (Tukey's HSD). NC = Normal Control, DC = Diabetic Control, LD = Low Dose, HD = High Dose, SD = Standard Drug.

The diabetic control group showed a pronounced atherogenic lipid profile with elevated total cholesterol, triglycerides, LDL-C, and reduced HDL-C. Both extract doses produced significant improvements across all lipid parameters. The high-dose group showed lipid values approaching those of the metformin group, and neither differed significantly from each other in total cholesterol or triglycerides.

4.5 Serum Insulin

Serum insulin levels were markedly reduced in the diabetic control group (1.8 ± 0.4 μ IU/mL) compared to the normal control group (14.7 ± 1.3 μ IU/mL), reflecting - streptozotocin induced beta cell destruction. Treatment with *S. cumini* extract at 400 mg/kg produced a statistically significant elevation in serum insulin (6.3 ± 0.9 μ IU/mL, $p < 0.01$ vs. diabetic control), suggesting partial functional recovery of pancreatic beta cells. The low-dose group showed a smaller but still significant improvement (4.2 ± 0.8 μ IU/mL, $p < 0.05$ vs. diabetic control). Metformin produced a slightly lower insulin improvement (5.8 ± 0.7 μ IU/mL), consistent with its known mechanism of action.

4.6 Oxidative Stress Markers

Table 3: Oxidative Stress Markers on Day 28

Parameter	NC	DC	LD (200 mg/kg)	HD (400 mg/kg)	SD (Metformin)
MDA (nmol/mL)	2.14 ± 0.18	8.73 ± 0.67	6.12 ± 0.48*	4.38 ± 0.39**	4.61 ± 0.41**
GSH (μ g/mL)	38.7 ± 2.9	14.2 ± 1.6	22.8 ± 2.3*	29.6 ± 2.7**	28.4 ± 2.5**

* $p < 0.05$ vs. Diabetic Control; ** $p < 0.01$ vs. Diabetic Control.

The marked elevation in MDA and depression in GSH in the diabetic control confirm significant oxidative stress in untreated hyperglycemia. *S. cumini* seed extract produced

dose-dependent reversal of both markers. The high-dose group achieved MDA levels (4.38 ± 0.39 nmol/mL) and GSH levels (29.6 ± 2.7 μ g/mL) statistically indistinguishable from the metformin group.

4.7 Correlation Analysis

Table 4: Pearson Correlation Coefficients (r) Between Blood Glucose and Other Parameters in Combined Treatment Groups (n = 18)

Variable	r Value	p-value	Interpretation
Serum Insulin	-0.87	< 0.001	Strong negative correlation
MDA	+0.91	< 0.001	Strong positive correlation
GSH	-0.83	< 0.001	Strong negative correlation
Total Cholesterol	+0.78	< 0.001	Moderate-strong positive
Triglycerides	+0.74	< 0.001	Moderate positive correlation
HDL-C	-0.69	0.001	Moderate negative correlation
Body Weight	-0.62	0.006	Moderate negative correlation

The correlation between blood glucose and MDA was the strongest positive relationship ($r = +0.91$, $p < 0.001$), confirming that as blood glucose decreased with treatment, oxidative stress markers fell in close proportion. The strong negative correlation between blood glucose and serum insulin ($r = -0.87$, $p < 0.001$) indicates that the glucose-lowering effect is meaningfully associated with insulin recovery, consistent with the hypothesis that the extract acts partly through beta cell protection and antioxidant mechanisms.

4.8 Histopathological Findings

Histopathological sections of pancreatic tissue from the normal control group showed well-defined islets of Langerhans with abundant beta cells, uniform morphology, and no signs of inflammation or necrosis. The diabetic control group displayed marked distortion of islet architecture, significant beta cell depletion, areas of necrosis, and inflammatory infiltration consistent with streptozotocin toxicity.

In the low-dose extract group, partial preservation of islet structure was observed with moderate beta cell density and reduced inflammatory infiltration. The high-dose group showed clearly better-defined islets, with visibly higher beta cell density, suggesting regenerative activity or protection from further - streptozotocin induced damage. The metformin group showed a similar histological picture to the high-dose extract group.

5. Discussion

The findings of this study carry several layers of significance. At the most basic level, they confirm what many in vitro and in vivo studies have suggested: that *Syzygium cumini* seed extract meaningfully reduces blood glucose, corrects lipid abnormalities, and ameliorates oxidative stress in streptozotocin induced diabetic mice. But the contribution of this study goes beyond simple replication. The application of regression analysis, correlation matrices, and formal hypothesis testing to these experimental data provides a richer picture of what is happening at the system level and how reliably the effects can be characterized.

The linear dose-response relationship ($R^2 = 0.983$) between extract dose and blood glucose on day 28 is a particularly important finding. It tells us that within the dose range tested, the extract behaves predictably, and that higher doses yield proportionally greater effects. This is not always the case with herbal extracts, some of which show bell-shaped dose-response curves or plateau effects at moderate doses. The linearity observed here is a favorable characteristic for eventual dosage optimization in preclinical and clinical studies.

The strong correlation between blood glucose and MDA ($r = +0.91$) deserves particular attention. Oxidative stress is widely recognized as both a consequence and a driver of diabetic hyperglycemia. itself ac streptozotocin by generating hydroxyl radicals within beta cells, which is why the antioxidant capacity of *S. cumini* is pharmacologically relevant. The polyphenolic compounds in the extract, particularly gallic acid and ellagic acid, are known free radical scavengers that replenish cellular antioxidant reserves. The fact that GSH levels were substantially restored in the high-dose group (29.6 $\mu\text{g/mL}$ vs. 14.2 $\mu\text{g/mL}$ in the diabetic control) suggests that the extract improves the cellular redox environment, which may in turn protect remaining beta cells and improve peripheral insulin signaling.

Comparison with metformin is instructive because it helps calibrate the clinical relevance of the extract's effects. Metformin primarily reduces hepatic glucose output by activating AMPK and does not substantially improve insulin secretion. The fact that the high-dose extract group showed comparable blood glucose reduction to metformin, while also demonstrating higher serum insulin levels, suggests that the extract's mechanism is at least partially different and potentially complementary. This raises the intriguing possibility that *S. cumini* extract could serve as an adjuvant to metformin in human patients, potentially allowing lower doses of metformin while maintaining glycemic control.

One aspect that merits reflection is the use of streptozotocin -induced diabetes as a model system. streptozotocin produces a state closer to Type 1 diabetes through direct beta cell destruction, while the majority of human diabetes is Type 2. Future work using high-fat diet-induced insulin resistance models would provide important complementary data. The streptozotocin model has the advantage of producing reliable and consistent hyperglycemia

and is widely used in the published literature on *S. cumini*, making results directly comparable to prior investigations.

6. Proposed Mechanisms of Action

The antidiabetic activity of *S. cumini* appears to proceed through at least four distinct but converging pathways, and understanding these separately helps explain why the effects are broad enough to influence glucose, lipid, and oxidative stress parameters simultaneously.

Pathway 1: Alpha-Glucosidase Inhibition

The seed extract contains gallic acid and kaempferol, both of which inhibit the intestinal enzyme alpha-glucosidase with IC₅₀ values comparable to or better than acarbose. By slowing the breakdown of complex carbohydrates in the small intestine, these compounds reduce the rate of glucose entry into the bloodstream after meals. Jamboline, the alkaloid unique to *S. cumini* seeds, further contributes by inhibiting the diastatic conversion of starch to glucose.

Pathway 2: Antioxidant Mechanism

Polyphenols in the extract, particularly ellagic acid and gallic acid, donate hydrogen atoms to neutralize reactive oxygen species. This reduces lipid peroxidation (reflected in lower MDA levels), preserves intracellular GSH, and upregulates endogenous antioxidant enzymes. In the context of streptozotocin -induced diabetes, this protective effect is particularly significant because it limits further damage to surviving beta cells.

Pathway 3: Anti-Glycation Effect

Ellagic acid has been demonstrated to inhibit the formation of carboxymethyl lysine (CML), the most abundant advanced glycation end-product (AGE) in diabetic patients, and to inhibit glycosylated hemoglobin (HbA1c) formation. This mechanism is clinically highly relevant for long-term complication prevention involving neuropathy, retinopathy, and nephropathy.

Pathway 4: Improvement of Insulin Signaling

Quercetin, present in *S. cumini* seeds, has been shown to activate tyrosine kinase activity associated with the insulin receptor, facilitating signal transduction downstream of receptor binding. Additionally, multiple bioactive compounds in the extract appear to enhance glucose uptake in peripheral tissues, as demonstrated by the fourfold increase in glucose uptake in L6 muscle cells reported by Syama et al. (2018). This insulin sensitization effect is

particularly relevant for Type 2 diabetic patients whose primary problem is inadequate cellular response to available insulin.

7. Conclusions

This study provides experimental evidence, supported by hypothesis testing, correlation analysis, and regression modeling, that ethanolic seed extract of *Syzygium cumini* exerts significant antidiabetic, antilipidemic, and antioxidant effects in streptozotocin -induced diabetic Swiss albino mice. At a dose of 400 mg/kg body weight, the extract achieved blood glucose reduction and lipid profile improvements comparable to metformin, while additionally showing greater improvement in serum insulin levels and oxidative stress markers, suggesting a broader spectrum of pharmacological action.

The dose-response regression confirms a predictable linear relationship between dose and therapeutic effect. Correlation analysis establishes that glucose reduction is tightly associated with simultaneous improvement in oxidative stress markers and insulin recovery, consistent with a mechanism involving beta cell protection and antioxidant activity rather than a single isolated pharmacological effect. Histopathological findings confirm structural preservation of pancreatic islets in extract-treated animals.

These results strongly support continued investigation of *S. cumini* seed extract as a candidate for adjuvant therapy in diabetes management. Future studies should examine effects in insulin-resistant, high-fat diet models, explore isolated active fractions individually and in combination, conduct longer-duration studies to assess chronic toxicity and efficacy, and ultimately move toward well-designed human clinical trials with adequate sample sizes and validated outcome measures.

The story of Jamun as an antidiabetic plant is one that bridges ancient observation and modern science in a genuinely productive way. What practitioners of Ayurveda and traditional medicine observed centuries ago about this fruit's effect on blood sugar is not magic or coincidence. It is biochemistry operating at multiple levels, and understanding that biochemistry with precision is now well within reach.

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