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EVALUATION OF ANTIDIABETIC ACTIVITY OF *MADHUCA LONGIFOLIA* FLOWER EXTRACT IN *INVIVO* STUDIES

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ABSTRACT

Aim: Diabetes mellitus is a major global metabolic disorder characterized by chronic hyperglycemia due to insufficient insulin secretion and/or action. The present study aimed to investigate the potential antidiabetic effects of a Madhuca longifolia flower extract on streptozotocin-induced diabetic rats, an established animal model for studying diabetes and its complications. **Methods:** Diabetes was induced in overnight-fasted Wistar rats by a single intraperitoneal injection of streptozotocin (STZ) at a dose of 50 mg/kg body weight and nicotinamide at dose of 100mg/kg, dissolved in a cold 0.1 M citrate buffer (pH 4.5). Rats with fasting blood glucose levels above 200 mg/dL after 72 hours were considered diabetic. Diabetic animals were divided into treatment groups and orally administered the plant extract (e.g., at doses of 200 mg/kg and 400 mg/kg body weight) or a standard antidiabetic drug, metformin(e.g., 5 mg/kg body weight), daily for a period of 28 days. Fasting blood glucose (FBG) levels, body weight, and various biochemical parameters lipid profile (total cholesterol, triglycerides, HDL, LDL), liver function markers (ALT, AST), kidney function markers (creatinine, BUN), will be analyzed. At the end of the study, pancreatic tissues were collected for histopathological examination. **Results:** Oral administration of the plant extract to diabetic rats for the treatment period resulted in a significant ($p < 0.05$) reduction in elevated FBG and lipid profile levels compared to the untreated diabetic control group. The extract treatment also prevented significant body weight loss and improved altered lipid profiles (e.g., decreased total cholesterol and triglycerides, increased HDL) and liver/kidney function parameters. Histopathological analysis of the pancreas from treated rats showed preservation and regeneration of pancreatic beta-cells compared to the severe necrosis and cellular damage observed in untreated diabetic rats. **Conclusion:** The findings suggest that the plant extract possesses significant antidiabetic protective effects against diabetes-associated complications in STZ-induced diabetic rats. Its efficacy was comparable to the standard drug metformin, thereby validating its potential as a natural therapeutic agent for diabetes management.

KEYWORDS: Anti-diabetic, Madhuca longifolia flower extract, Streptozotozin-nicotinamide induced diabetes, blood glucose level, oral glucose tolerance test, body weight, lipid profile, ALT, AST, Creatinine, BUN.

1. INTRODUCTION

Diabetes is a widespread chronic metabolic disorder characterized by insulin resistance and relative insulin deficiency. Unlike Type 1 diabetes, which results from the autoimmune destruction of insulin-producing beta cells in the pancreas, Type 2 diabetes develops gradually and is often linked to lifestyle factors such as obesity, physical inactivity, and poor dietary habits. Type 2 diabetes accounts for the majority of diabetes cases globally and poses significant challenges due to its potential to cause complications affecting multiple organ systems. Effective management involves lifestyle modifications, pharmacological interventions, and continuous blood sugar monitoring to minimize the risk of long-term complications.[1,2]

2. Plant profile[3,4,5]

Taxonomical Classification Kingdom: Plantae

Phylum: Angiosperm

Class: Eudicot

Order: Ericales

Family: Sapotacea

Genus: Madhuca

Species: *Madhuca longifolia*

Fig. 1: Flowers of *Madhuca longifolia.*

3. MATERIALS AND METHODS

3.1. Collection, Authentication and Extract Preparation

The flowers of *Madhuca longifolia* were sourced from A. Sembulichampalayam, Anthiyur, Erode, Tamilnadu and authenticated to confirm their botanical identity. The palnt authentication number M120625034L .After authentication, the flowers were thoroughly cleaned, shade-dried, and ground into a fine powder. A total of 100 grams of the powdered material was subjected to extraction using ethanol as a solvent. The powdered flowers were extracted using soxhlet apparatus in 500 mL of ethanol for 8 hours at room temperature with intermittent shaking. After the extraction period, the mixture was filtered using Whatman No. 1 filter paper to remove plant residues. The filtrate was then concentrated using a rotary evaporator under reduced pressure at 40°C until a semi-solid residue was obtained. The dried extract was collected, weighed, and stored in an airtight container at 4°C for further in vivo studies.[6,7,8]

3.2. In-vivo anti-diabetic activity

Male Wistar albino rats (180–220 g) will be housed under standard laboratory conditions (22± 2°C, 12-hour light/dark cycle) with ad libitum access to food and water and acclimatized for one week. Diabetes will be induced by intraperitoneal injection of streptozotocin and nicotinamide at a dose of 50 mg/kg and 100 mg/kg BW, prepared freshly in 0.1 M cold citrate buffer (pH 4.5). To prevent hypoglycemia, rats will receive 5% glucose solution for 24 hours. After 72 hours (3 days), fasting blood glucose (FBG) levels will be measured, and rats with FBG ≥ 200 mg/dL will be considered diabetic. The animals will be divided into five groups: Group I (Normal Control) receiving distilled water, Group II (Negative Control) receiving STZ+ NAD alone, Group III receiving Metformin (100 mg/kg, orally), Group IV receiving *Madhuca longifolia* flower extract (200 mg/kg, orally), and Group V receiving *Madhuca longifolia* flower extract (400 mg/kg, orally). Treatments will be administered daily for 28 days (0, 7th, 14th, 21st, 28th). Body weight and fasting blood glucose levels will be monitored weekly, while an oral glucose tolerance test (OGTT) will be performed on day 29. Serum biochemical parameters, including lipid profile (total cholesterol, triglycerides, HDL, LDL), liver function markers (ALT, AST), kidney function markers (creatinine, BUN), will be analyzed.[9,10]

Statistical analysis

The results will be analyzed for statistical significance using one-way ANOVA followed by Dunnett's test. P Values<0.05 were considered significant.

4. RESULT

4.1. Evaluation of fasting blood glucose after treatment

Day 0

At the commencement of the study, fasting blood glucose (FBG) levels were measured across all groups to establish a baseline prior to any treatment intervention. Group I, the normal control group receiving only normal saline, displayed normoglycemic levels at 87.3 ± 3.2 mg/dL, consistent with healthy, non-diabetic animals. Groups II to V, which received a single intraperitoneal dose of STZ + NAD to induce diabetes, showed significantly elevated glucose levels ranging from 273.8 ± 5.6 to 276.9 ± 5.7 mg/dL. This sharp rise in blood glucose post- STZ + NAD administration confirms the successful induction of hyperglycemia and serves as a reliable model for evaluating the anti-diabetic potential of therapeutic agents. Importantly, no significant differences were observed among the diabetic groups at baseline, ensuring uniformity and comparability for subsequent time-point evaluations.

Day 7

One week following STZ + NAD induction and subsequent treatment initiation, noticeable differences in FBG levels began to emerge among the groups. Group II (diabetic control) exhibited a further elevation in blood glucose to 318.4 ± 8.3 mg/dL, indicating the progressive nature of hyperglycemia in untreated diabetic animals. In contrast, Group III, treated with metformin (100 mg/kg), demonstrated a marked decline in glucose levels to 214.7 ± 5.2 mg/dL, highlighting the early onset of metformin's antihyperglycemic action through improved peripheral glucose uptake and hepatic gluconeogenesis inhibition. The groups treated with *Madhuca longifolia* flower extract began to show promising glycemic control as well. Group IV (200 mg/kg) reduced to 244.1 ± 5.9 mg/dL, and Group V (400 mg/kg) to 229.4 ± 5.2 mg/dL, suggesting a dose-dependent initial glucose-lowering effect. Although not as potent as metformin at this stage, the results indicate that EEML may modulate blood glucose levels through mechanisms that require gradual biological interaction, possibly involving insulin sensitization or inhibition of carbohydrate-digesting enzymes.

Day 14

By the second week, therapeutic outcomes became more pronounced. The diabetic control group (Group II) continued to exhibit elevated glucose levels (326.2 ± 6.7 mg/dL), reinforcing the chronic progression of hyperglycemia in the absence of treatment. In contrast, metformin- treated Group III showed a continued and substantial reduction in FBG to 169.3 ± 4.6 mg/dL, reflecting the sustained pharmacodynamic effects of metformin. Both extract-treated groups also demonstrated notable improvements. Group IV (200 mg/kg) showed a further decreases 210.6 ± 5.4 mg/dL, while Group V (400 mg/kg) reached 185.8 ± 4.8 mg/dL, bringing it closer to the metformin group. The results at this point underscore the extract's ability to gradually normalize blood glucose levels, especially at higher doses. These effects may be attributed to the accumulation of bioactive compounds acting on multiple glycemic control pathways, such as pancreatic β-cell preservation or modulation of glucose metabolism enzymes.

Day 21

On day 21, the therapeutic benefits of both standard and extract treatments became more evident. Group II, left untreated, continued its upward glycemic trajectory with FBG reaching 330.5 ± 7.1 mg/dL, confirming the persistent diabetic state. Conversely, Group III showed a significant decline to 136.8 ± 4.4 mg/dL, nearing normoglycemic values, indicating metformin's maximal efficacy. Group IV (200 mg/kg EEML) dropped further to 178.9 ± 4.7 mg/dL, while Group V (400 mg/kg) reached 151.7 ± 4.2 mg/dL, suggesting strong dose-related efficacy of the extract. The progressive improvement in these groups supports the hypothesis that *Madhuca longifolia* exerts its antihyperglycemic effect through cumulative action, likely involving enzyme inhibition (such as α-amylase or α-glucosidase) and/or improved glucose utilization. The 400 mg/kg dose, in particular, displayed remarkable potential to regulate glycemia effectively, demonstrating outcomes nearly equivalent to those of the standard drug.

Day 28

At the end of the 28-day study, the differences among the treatment groups were highly significant. The untreated diabetic group (Group II) maintained high FBG levels (336.8 ± 6.9 mg/dL), confirming disease progression without intervention. Group III (metformin) achieved near-normal glucose levels at 115.5 ± 3.8 mg/dL, confirming its robust glucose-lowering capacity. Group IV, receiving 200 mg/kg of EEML, recorded an FBG of 148.7 ± 3.9 mg/dL, indicating moderate glycemic control. Impressively, Group V (400 mg/kg) exhibited FBG levels at 122.3 ± 3.6 mg/dL, approaching those seen in the metformin-treated group. These results strongly support the potential of *Madhuca longifolia* flower extract in managing diabetes, especially at higher doses. The prolonged and consistent decline in blood glucose levels highlights the extract's probable role in pancreatic function improvement, peripheral insulin sensitivity, or suppression of glucose absorption. The data affirm its suitability for future development as a natural anti-diabetic agent.

Table 1: Estimation of fasting blood glucose level in rats.

Group	Day 0	Day 7	Day 14	Day 21	Day 28
Group I	87.3 ± 3.2	88.6 ± 2.9	89.1 ± 3.1	87.9 ± 2.7	88.2 ± 2.5
Group II	273.8 ± 5.6	318.4 ± 8.3	326.2 ± 6.7	330.5 ± 7.1	336.8 ± 6.9
Group III	275.6 ± 4.8	214.7 ± 5.2 **	169.3 ± 4.6 **	136.8 ± 4.4 **	115.5 ± 3.8 **
Group IV	278.2 ± 6.1	244.1 ± 5.9 *	210.6 ± 5.4 *	178.9 ± 4.7 *	148.7 ± 3.9 *
Group V	276.9 ± 5.7	229.4 ± 5.2 **	185.8 ± 4.8 **	151.7 ± 4.2 **	122.3 ± 3.6 **

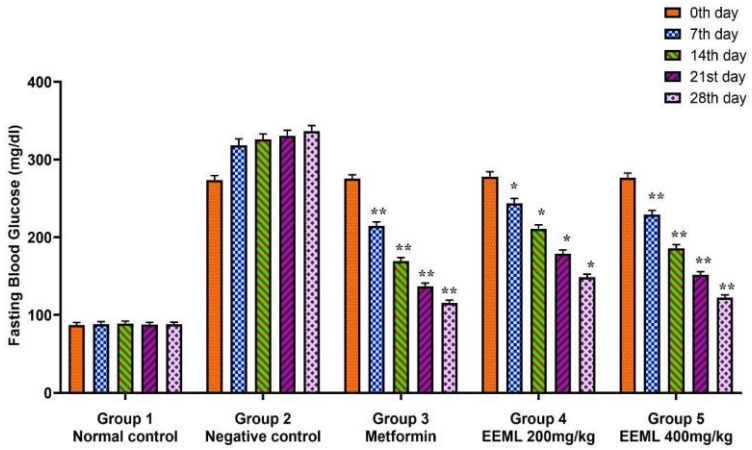


Fig. 2: Effect of EEML on fasting blood glucose levels in rat.

4.2. Evaluation of body weight

Monitoring body weight is a crucial parameter in evaluating the physiological impact of diabetes and the therapeutic efficacy of anti-diabetic agents. In the present study, a consistent increase in body weight was observed in the normal control group (Group I), ranging from 222.35 ± 2.96 g on Day 0 to 233.49 ± 1.54 g on Day 28. This trend reflects normal growth in healthy rats with no metabolic disturbances. In contrast, the negative control group (Group II), which received STZ + NAD to induce diabetes, demonstrated a progressive and significant decline in body weight from 216.57 ± 1.87 g at baseline to 202.41 ± 2.23 g by Day 28. This weight loss is a typical consequence of STZ + NAD - induced diabetes, primarily due to insulin deficiency, enhanced muscle protein breakdown, and impaired glucose utilization.

Table 2: Estimation of body weight changes in rats.

Day	Group I (Normal Control)	Group II (Negative Control)	Group III (Metformin 100 mg/kg)	Group IV (EEML 200 mg/kg)	Group V (EEML 400 mg/kg)
0	222.35 ± 2.96	216.57 ±1.87	227.10 ± 1.90	214.73 ± 2.49	223.86 ± 1.68
7	223.87 ± 1.81	213.59 ± 2.36	228.64 ± 1.59	213.96 ± 2.12	221.68 ± 2.04
14	227.80 ± 1.62	207.68 ± 2.08	225.22 ± 2.72	210.17 ± 2.54	220.11 ± 3.16
21	230.26 ± 2.92	204.83 ± 2.08	222.98 ± 1.70	208.31 ± 3.44	219.35 ± 2.59
28	233.49 ± 1.54	202.41 ± 2.23	223.28 ± 2.87	208.09 ± 3.05	218.81 ± 1.78

Evaluation of lipid profile

a) High-Density Lipoprotein (HDL)

In the present study, HDL levels were significantly reduced in diabetic control rats (Group II), dropping to 34.7 ± 2.1 mg/dL compared to the normal control (Group I), which maintained healthy HDL levels at 64.3 ± 2.5 mg/dL. This decline in HDL is a hallmark of diabetic dyslipidemia and reflects impaired reverse cholesterol transport and increased oxidative stress. Metformin-treated rats (Group III) exhibited a partial recovery of HDL to 58.9 ± 2.4 mg/dL. aligning with its known ability to improve lipid metabolism. Notably, *Madhuca longifolia* flower extract demonstrated a dose-dependent improvement in HDL levels, with 200 mg/kg (Group IV) increasing HDL to 51.6 ± 2.6 mg/dL and 400 mg/kg (Group V) significantly elevating it to 57.2 ± 2.3 mg/dL. These findings suggest that the extract may stimulate HDL biosynthesis or enhance its stability, thereby improving lipid homeostasis in diabetic conditions.

Table 3: Estimation of lipid profile.

Group	HDL (mg/dL)	LDL (mg/dL)	Triglycerides (mg/dL)	Total Cholesterol (mg/dL)
Group I (Normal Control)	64.3 ± 2.5	41.8 ± 3.6	88.4 ± 5.1	123.2 ± 4.7
Group II (Diabetic Control)	34.7 ± 2.1	78.6 ± 4.9	164.2 ± 6.3	197.8 ± 5.2
Group III (Metformin 100 mg/kg)	58.9 ± 2.4 *	48.2 ± 4.2 *	103.7 ± 5.6 *	137.4 ± 4.9 *
Group IV (EEML 200 mg/kg)	51.6 ± 2.6 *	55.9 ± 4.5 *	118.3 ± 5.9 *	148.6 ± 5.1 *
Group V (EEML 400 mg/kg)	57.2 ± 2.3 *	50.6 ± 4.1 *	107.9 ± 5.4 *	139.7 ± 4.8 *

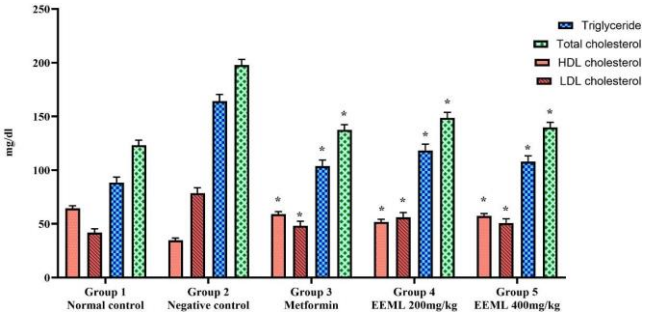


Fig. 3: Effect of EEML on the lipids.

b) Low-Density Lipoprotein (LDL)

LDL levels were markedly elevated in diabetic control rats (Group II) to 78.6 ± 4.9 mg/dL, indicating increased risk for atherosclerotic complications. This increase is likely due to hepatic overproduction of VLDL and reduced clearance of LDL particles, commonly seen in insulin- deficient states. Treatment with metformin (Group III) significantly reduced LDL to 48.2 ± 4.2 mg/dL, highlighting its efficacy in lowering atherogenic lipoproteins. Administration of *M. longifolia* extract at 200 mg/kg (Group IV) showed moderate LDL reduction to 55.9 ± 4.5 mg/dL, while the 400 mg/kg dose (Group V) further lowered LDL to 50.6 ± 4.1 mg/dL. These improvements may be attributed to the extract's ability to modulate lipid metabolism enzymes or enhance LDL receptor-mediated clearance, thereby mitigating cardiovascular risks associated with diabetes.

c) Triglycerides

A significant rise in triglyceride levels was observed in the diabetic control group (Group II), reaching 164.2 ± 6.3 mg/dL compared to 88.4 ± 5.1 mg/dL in the normal control group. This elevation reflects increased hepatic triglyceride synthesis and reduced lipoprotein lipase activity, common in insulin-deficient states. Metformin treatment (Group III) reduced triglycerides to 103.7 ± 5.6 mg/dL, aligning with its known inhibitory effects on hepatic gluconeogenesis and lipogenesis. The *M. longifolia* extract also showed promising effects— Group IV (200 mg/kg) recorded 118.3 ± 5.9 mg/dL, while Group V (400 mg/kg) showed a more substantial reduction to 107.9 ± 5.4 mg/dL. This triglyceride-lowering effect may stem from improved insulin sensitivity, enhanced fatty acid oxidation, or inhibition of de novo lipogenesis by phytochemicals in the extract.

d) Total Cholesterol

Total cholesterol levels followed a similar pattern, with diabetic rats (Group II) showing a marked increase to 197.8 ± 5.2 mg/dL, indicating disrupted lipid homeostasis and increased cardiovascular risk. This elevation is likely due to enhanced synthesis and impaired clearance of cholesterol-rich lipoproteins. Metformin-treated rats (Group III) showed significant cholesterol reduction to 137.4 ± 4.9 mg/dL, confirming its lipid-lowering potential. The 200 mg/kg dose of *M. longifolia* extract (Group IV) moderately reduced cholesterol to 148.6 ± 5.1 mg/dL, while the higher dose (Group V)

brought it down further to 139.7 ± 4.8 mg/dL. These results suggest the extract's potential role in modulating key enzymes like HMG-CoA reductase or increasing bile acid excretion, contributing to improved cholesterol management in diabetic rats.

Evaluation of biochemical parameters

a) Alanine Aminotransferase (ALT)

ALT is a key liver enzyme that serves as a sensitive marker of hepatocellular injury. In the present study, a significant elevation in ALT levels was observed in the diabetic control group (78.6 ± 3.4 U/L), exceeding the normal physiological range of 13–56 U/L for Albino rats, indicating considerable liver damage induced by streptozotocin (STZ + NAD). STZ is known to exert hepatotoxic effects through oxidative stress and inflammatory responses, contributing to altered membrane permeability and enzyme leakage into the bloodstream. Metformin treatment (Group III) effectively reduced ALT levels to 51.2 ± 2.3 U/L, restoring them within the normal range, likely due to its known antioxidant and anti-inflammatory effects that mitigate STZ-induced hepatic damage.Similarly, the higher dose of *Madhuca longifolia* flower extract (Group V) significantly lowered ALT to 47.6 ± 2.0 U/L, demonstrating hepatoprotective potential comparable to the standard. The 200 mg/kg dose (Group IV) resulted in a modest improvement (60.8 ± 2.9 U/L), suggesting a dose-dependent liver-protective effect of the extract. These findings imply that *M. longifolia* may aid in preserving hepatic integrity in diabetic conditions.

b) Aspartate Aminotransferase (AST)

AST, another hepatic enzyme, is present in various tissues including liver, heart, and skeletal muscle, making it a less liver-specific but important marker of tissue injury. The STZ + NAD-induced diabetic group showed a significant rise in AST levels (135.8 ± 4.6 U/L), reflecting generalized cellular damage. This elevation correlates with the observed hepatic dysfunctionand may also indicate STZ-induced extrahepatic tissue injury. Treatment with metformin (Group III) brought AST down to 89.2 ± 3.2 U/L, demonstrating its capacity to reduce systemic oxidative and inflammatory stress. Notably, the higher dose of *M. longifolia* extract (400 mg/kg) led to a marked reduction in AST levels (92.6 ± 3.1 U/L), while the 200 mg/kg dose brought AST to 104.3 ± 3.7 U/L. These results support the notion that *M. longifolia* possesses therapeutic properties capable of ameliorating enzyme leakage and possibly stabilizing cellular membranes. The extract's efficacy may stem from its natural bioactives that attenuate oxidative damage, which is crucial in managing diabetes-induced hepatic and systemic stress.

c) Creatinine

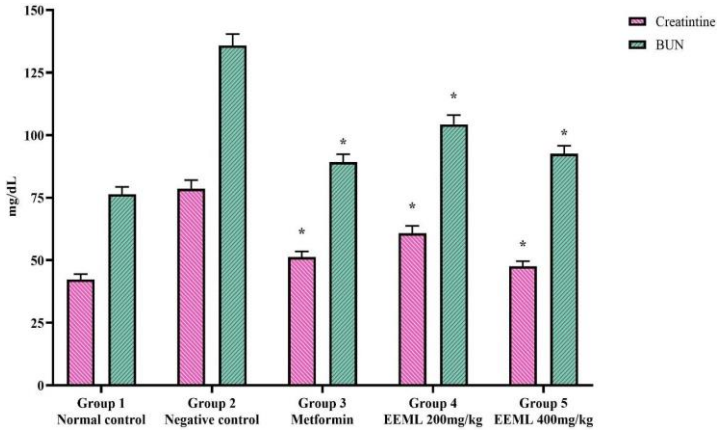
Serum creatinine is a reliable indicator of renal function, with elevated levels signifying impaired kidney filtration capacity. The diabetic control rats exhibited a significant increase in creatinine levels (1.34 ± 0.05 mg/dL), suggesting nephrotoxicity induced by chronic hyperglycemia and STZ. This renal impairment is often attributed to glomerular and tubular damage, leading to accumulation of nitrogenous waste in the blood. Metformin administration (Group III) effectively reduced creatinine levels to 0.74 ± 0.04 mg/dL, reflecting its nephroprotective action. Treatment with *M. longifolia* extract at 400 mg/kg (Group V) significantly ameliorated creatinine levels to 0.82 ± 0.03 mg/dL, nearly restoring them to normal. The lower dose (Group IV) showed a moderate effect (1.05 ± 0.04 mg/dL). These outcomes point to the renal protective potential of the extract, possibly through its antioxidant properties that protect the renal microvasculature from STZ-induced damage. The findings highlight the efficacy of *M. longifolia* in safeguarding renal function in diabetic conditions.

d) Blood Urea Nitrogen (BUN)

BUN is a measure of nitrogenous waste products and reflects both renal and hepatic function. A sharp rise in BUN levels was observed in the diabetic control group (42.3 ± 1.7 mg/dL), indicating renal dysfunction possibly due to glomerular damage and increased protein catabolism associated with uncontrolled diabetes. Metformin treatment significantly decreased BUN levels to 22.5 ± 1.3 mg/dL, reinforcing its known renoprotective capabilities. The *M. longifolia* extract also demonstrated beneficial effects: the higher dose (400 mg/kg) reduced BUN to 26.2 ± 1.1 mg/dL, while the lower dose (200 mg/kg) achieved a partial reduction to 31.7 ± 1.4 mg/dL. These improvements suggest that the extract supports nitrogen metabolism.

Estimation of biochemical parameters

Group	ALT (U/L)	AST (U/L)	Creatinine (mg/dL)	BUN (mg/dL)
Group I (Normal Control)	42.3 ± 2.1	76.4 ± 2.9	0.62 ± 0.03	18.7 ± 1.2
Group II (Diabetic Control)	78.6 ± 3.4	135.8 ± 4.6	1.34 ± 0.05	42.3 ± 1.7
Group III (Metformin 100 mg/kg)	51.2 ± 2.3 *	89.2 ± 3.2 *	0.74 ± 0.04 *	22.5 ± 1.3 *
Group IV (EEML 200 mg/kg)	60.8 ± 2.9 *	104.3 ± 3.7 *	1.05 ± 0.04 *	31.7 ± 1.4 *
Group V (EEML 400 mg/kg)	47.6 ± 2.0 *	92.6 ± 3.1 *	0.82 ± 0.03 *	26.2 ± 1.1 *



5. SUMMARY AND CONCLUSION

The present study investigated the antidiabetic potential of *Madhuca longifolia* flower extract through a in vivo studies, highlighting its multifaceted efficacy in managing hyperglycemia and associated metabolic dysfunctions.Phytochemical analysis confirmed the presence of flavonoids, phenolics, tannins, and saponins—phytoconstituents well-known for their antioxidant and metabolic regulatory roles. The ethanolic extract exhibited the highest yield (25.36%), prompting its selection for further biological evaluations. In vivo, the streptozotocin (STZ)-induced diabetic rat model displayed consistent signs of diabetes, including hyperglycemia, weight loss, impaired glucose tolerance, and dyslipidemia. Over the 28-day treatment period, animals receiving *Madhuca longifolia* extract exhibited significant improvements in multiple metabolic parameters.Fasting blood glucose (FBG) levels decreased progressively from 276.9 ± 5.7 mg/dL at baseline to 122.3 ± 3.6 mg/dL at day 28 in the high-dose extract group (400 mg/kg), closely approximating the metformin-treated group (115.5 ± 3.8 mg/dL).This reduction was statistically significant (**$p<0.01$) compared to the diabetic control group and demonstrates the glucose-lowering efficacy of the extract. OGTT results further confirmed this, as the high-dose extract group showed significantly reduced glucose levels at 60 and 120 minutes, indicative of enhanced glucose tolerance and improved insulin sensitivity.Lipid profile parameters showed marked improvement in treated groups. The high-dose group demonstrated a significant reduction in LDL (50.6 ± 4.1 mg/dL) and triglycerides

(107.9 ± 5.4 mg/dL), along with an increase in HDL (57.2 ± 2.3 mg/dL) when compared to diabetic controls. These changes underscore the extract's potential to mitigate diabetic dyslipidemia and reduce cardiovascular risk. The total cholesterol levels in the high-dose extract group were brought down to 139.7 ± 4.8 mg/dL, nearly matching the metformin group.Hepatoprotective effects were evident through the normalization of liver enzyme levels. ALT and AST levels, which were elevated in diabetic control rats (78.6 ± 3.4 and 135.8 ± 4.6 IU/L, respectively), were significantly reduced in extract-treated groups, particularly in the high-dose group (47.6 ± 2.0 and 92.6 ± 3.1 IU/L), indicating reduced hepatic stress or injury.Similarly, kidney function markers—creatinine and BUN—were restored toward normalcy in the high-dose group, measuring 0.82 ± 0.03 mg/dL and 26.2 ± 1.1 mg/dL, respectively, against elevated values in the diabetic control group. These improvements suggest nephroprotective potential, possibly due to reduced glycotoxicity and oxidative stress.Overall, the findings reveal that *Madhuca longifolia* extract not only exerts antihyperglycemic activity but also contributes to comprehensive metabolic regulation, tissue protection, and restoration of physiological balance disrupted in diabetes.The 28-day in vivo study further confirmed its therapeutic role by significantly lowering fasting blood glucose and improving glucose tolerance, lipid profile, liver and kidney function, and body weight in diabetic Albino rats.The plausible mechanism involves a synergistic action of the extract's bioactive phytoconstituents, particularly flavonoids and phenolics, which may exert antioxidant effects, inhibit carbohydrate-hydrolyzing enzymes, modulate insulin sensitivity, and protect vital organs from STZ-induced damage.These findings not only affirm the ethnomedicinal use of *Madhuca longifolia* in traditional diabetes management but also underscore its potential for development as a plant-based adjunct or alternative to current antidiabetic therapies.[11,12]

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