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Investigation of the *in-vitro* and *in-vivo* hypoglycemic potential of *musa paradisiaca* l. (ab) and *mangifera indica* l. Inflorescences

Silpa IS*, Akila E, Krishna Murthy, Neha KB, Kashifa Farheen

ABSTRACT

Objective: This study aims to investigate the hypoglycemic effects of the inflorescences of *Musa paradisiaca* L. (AB) and *Mangifera indica* L., exploring their in-vitro and in-vivo antidiabetic potential. *Methods:* The study involved alpha-amylase and alpha-glucosidase inhibition assays to evaluate in-vitro antidiabetic properties, followed by in-vivo testing using diabetic Wistar rats treated with ethanolic extracts of the plants. Critical parameters measured included blood glucose levels, body weight, and lipid profiles. Histopathological analysis was also conducted to assess tissue recovery. *Results:* Ethanolic extracts of both plants showed significant inhibition in enzyme assays, indicating potential antidiabetic properties. In diabetic rat models, high doses of the extracts significantly reduced blood glucose levels, improved lipid profiles, and enhanced body weight. Histopathological findings revealed notable recovery in pancreatic and liver tissues. *Conclusion: Musa paradisiaca* L. (AB) and *Mangifera indica* L. inflorescences demonstrate considerable antidiabetic effects, with potential for use in diabetes management due to their ability to lower glucose levels, improve lipid metabolism, and support tissue recovery.

Keywords: *Musa paradisiaca* L., *Mangifera indica* L., hypoglycemic activity, *diabetes mellitus*.

1. INTRODUCTION

A state of hyperglycemia during fasting or after meals is known as *diabetes mellitus*. Diabetes means "to pass through" in Greek, and the Latin word for honey, "mellitus", denotes sweetness. Diabetes is a long-term condition brought on by either insufficient insulin production by the pancreas or inefficient insulin use by the body. Uncontrolled diabetes frequently results in hyperglycemia, also known as elevated blood glucose or elevated blood sugar, which over time causes serious harm to numerous bodily systems, including the blood vessels and neurons (Alam et al., 2014; Shaw et al., 2010). Insulin resistance and β-cell dysfunction are the two primary problems of type 2 *diabetes mellitus* (T2DM). Disruptions in cellular pathways,

particularly in adipose tissue, result in insulin resistance by decreasing the sensitivity of cells to insulin. To maintain regular blood sugar, this resistance first causes cells to produce more insulin (hyperinsulinemia).

Eventually, β-cells cannot keep up, which results in insulin insufficiency and ultimately hyperglycemia (Banday et al., 2020). The adverse effects of oral hypoglycemic medications have increased interest in herbal treatments for diabetes. Herbs used in traditional Ayurvedic medicine help manage diabetes by enhancing digestion, regulating stomach secretions, and lowering body fluids like sweat and urine. The benefits of madhumehaghna,' or foods with antidiabetic qualities, in regulating metabolic imbalances are highlighted. Barley, ancient grains, legumes, drumstick leaves, bitter gourd, jamun, amla, and raw papaya are a few examples. These provide extra health benefits in controlling diabetes and associated complications, even if they might not drop blood sugar as well as drugs (Jarald et al., 2008).

Musa paradisiaca L. (AB) is a hybrid clone of *Musa acuminata* and *Musa balbisiana* belonging to the family Musaceae. It is native to Kerala and is referred to locally as Kannan variations. After being dried and powdered, the raw fruits are utilized as infant food. Asians frequently use the blooms beneath the bracts and the white inner portion (stalk) of the inflorescence (spadix) as dietary items. *Musa paradisiaca* L. is prized for its nutritional and therapeutic qualities and is commonly grown in tropical areas. Several plant parts, such as the stem, peel, and leaves, are used in traditional medicine to treat conditions like diabetes, high blood pressure, and ulcers and are a staple diet. Its inflorescence first appears as a big, tapered, purple bud before emerging as a terminal spike from the apex of the stem. It exposes two rows of white, nectar-rich blooms, each cluster surrounded by a thick, waxy bract that is deep crimson within and purple on the outside.

Male flowers are found in the top rows, while female flowers are found in the lower rows. Hermaphrodite or neutral blooms may be found in some rows. A "hand" of bananas is formed as the developing fruit bends the stalk as the bracts fall away (Singhal et al., 2022). *Mangifera indica* L. (Anacardiaceae), commonly known as mango, is one of the world's most important tropical fruits, with India as a top producer. In India, mango is celebrated as the "king of fruits", and various parts of *M. indica* are used medicinally across the globe Tharanathan et al., (2006) Mangiferin, a C-glucosyl xanthone and polyphenolic anti-oxidant, possesses potent anti-oxidant, immunomodulatory, cardiotonic, hypotensive, wound-healing, antidegenerative, and antidiabetic properties.

For vitiated disorders such as pitta, haemorrhages, haemoptysis, wounds, ulcers, anorexia, dyspepsia, oedema gleet, bladder catarrh, diarrhoea, chronic dysentery, and anaemia, the dried flowers are beneficial. It contains calcium, magnesium, potassium, sodium, phosphorus, iron, and other minerals. It is also a vital source of vitamins A, B, and C. Mango blossoms have been shown to possess astringent and antibacterial qualities (Kalita, 2014; Hussain et al., 2021). The subsessile, fragrant flowers measure 6 to 8 mm in diameter. The pollen grains vary in size, ranging from 20 to 35 microns. On a single panicle, both male and hermaphrodite blooms develop, with more males (Parvez, 2016).

2. MATERIALS AND METHODS

Plant material collection

Musa paradisiaca L(AB) and *Mangifera indica* L.'s inflorescence were collected from a home garden in Thrissur, Kerala, India. The sample drug has been identified and authenticated by DR. V. Rama Rao, Central Ayurveda Research Institute, Bengaluru, Karnataka.

Preparation of extracts

Musa paradisiaca L. (AB) and *Mangifera indica* L. Fresh inflorescences were shade-dried for 20 days, ground coarsely in a mechanical grinder, and sieved through a #10 mesh screen. An airtight container was then used to keep the powders. A Soxhlet apparatus extracted 50 grams of dried, powdered inflorescences. The thimble was then heated and refluxed with petroleum ether for 6–8 hours until the solvent in the siphon tube turned clear. After being dried and stored, the extract was concentrated using a rotary evaporator. The plant material residue was dried before the extraction was repeated using chloroform and refluxed for 6–8 hours. The extract was then recovered and dried as previously. This process was repeated for ethanol extraction, using the same reflux and drying methods. For water extraction, the dried plant residue underwent cold maceration.

***Invitro*-anti-diabetic activity**

Alpha-amylase inhibition assay

To assess α-amylase inhibition, add 0.5 mL of α-amylase solution (0.5 mg/mL) to the test extract, then incubate this mixture for 10 minutes at 25°C. Next, add 0.5 mL of sodium phosphate buffer (0.02 M) containing 1% starch to the mixture and incubate again for the specified time at 25°C. To halt the enzymatic activity, immediately add 1 mL of DNSA reagent and boil the reaction mixture at 95°C for 5 minutes. Allow the tubes to cool, then bring the final volume to 10 mL by adding distilled water. Measure the absorbance of the solution at 540 nm using a spectrophotometer and compare it to the acarbose standard to evaluate α-amylase inhibition (Thalapaneni et al., 2008; Heidari et al., 2005).

Alpha-glucosidase inhibition assay

In a test tube, combine 1 mL of a 2% starch solution with 0.2 M Tris buffer (pH 8) and the prepared sample (100-400 mg/mL), then incubate the mixture at 37°C for 10 minutes. Then, add 1 mL of α-glucosidase enzyme solution (1 U/mL) and incubate at 35°C for 40 minutes. Fill each tube with 2 mL of 6 N HCl to halt the process. A spectrophotometer measures the mixture's absorbance at 540 nm. (Andrade-Cetto et al., 2008; Matsuura et al., 2002).

Calculation of 50% Inhibitory Concentration (IC50)

The percentage inhibition (I%) is calculated using the formula:

%Inhibitory Activity = (Ac-As)/Ac ×100

Where: Ac = absorbance of the control (without the test sample)

As = absorbance of the sample

***In-vivo* antidiabetic activity**

Experimental animals

In the investigation, male Wistar rats weighing between 190 and 200 g were employed. The experimental mice were kept at room temperature with a photoperiod of 12 hours of light and 12 hours of darkness. They were given water and regular mouse pellets.

Induction of non-insulin-dependent (Type 2) diabetes mellitus

Male rats that had fasted overnight were given a single intraperitoneal injection of 60 mg/kg STZ 15 minutes after receiving 120 mg/kg nicotinamide intraperitoneally (i.p.) to develop non-insulin-dependent diabetic mellitus (NIDDM). The raised blood glucose level, measured 72 hours on days 7 and 10 following injection, will confirm hyperglycemia. For the antidiabetic research, rats with persistent NIDDM (> 250 mg/dl) on day ten were used. The standard will be glibenclamide (Chandran et al., 2016).

Acute toxicity studies

Five rats were used for acute toxicity studies. Per Organisation for Economic Development (OECD) guideline no.423, they will be dosed at 2000 mg/kg. One animal at a time was selected, weighed, and given a dose of extract diluted in distilled water in an equal volume (2000 mg/kg). The animals were housed in distinct metabolic cages and watched for signs and symptoms for five minutes. After that, they were watched every fifteen minutes for the first four hours after the dose, every thirty minutes for six hours, and every forty-eight hours every day for fourteen days. On days 1, 7, and 14, body weight is then measured (Shirwaikar et al., 2005).

Experimental design

The experimental design was conducted in seven groups, containing six animals each. Group 1 served as the control and received only the vehicle at a dose of 10 mL/kg of body weight daily for three weeks through oral administration. Group 2 was treated with STZ (streptozotocin) and nicotinamide, receiving a single intraperitoneal injection of 60 mg/kg of STZ, administered 15 minutes after an intraperitoneal injection of 120 mg/kg of nicotinamide. Group 3 received the same STZ and Nicotinamide treatment, along with the standard glibenclamide, administered as a single 60 mg/kg intraperitoneal injection followed by 10 mg/kg of glibenclamide daily via oral administration.

Group 4 was administered a low dose of ethanolic extract from the inflorescences of Musa *paradisiaca* L. (AB) daily for 3 weeks in diabetic rats, while group 5 received a high dose of the same extract daily for three weeks. Group 6 was given a low dose of ethanolic extract from the inflorescences of *Mangifera indica* L. daily for three weeks. Group 7 received a high dose of *Mangifera indica* L. extract daily for three weeks in diabetic rats. This setup allowed for comparison between different treatments and dosages in managing diabetes.

3. RESULTS & DISCUSSION

Extraction

The inflorescences of *Musa paradisiaca* L(AB) and *Mangifera indica* L were subjected to an extraction process using various solvents, including petroleum ether, chloroform, and ethanol through the Soxhlet extraction method, followed by water by cold maceration. The resulting extracts were concentrated using a rotary flash evaporator.

Alpha-Amylase Inhibition Assay

The alpha-amylase inhibition assay measures how well the substance inhibits the alpha-amylase enzyme, assessing its potential antidiabetic effects. This technique aids in discovering substances that, by delaying the digestion of carbohydrates, may help control blood sugar. Here, a spectrophotometer was used to measure the absorbance at 540 nm to compute the alpha-amylase inhibition percentage for *Musa paradisiaca* L (AB) and *Mangifera indica* L inflorescences. Acarbose was the standard in this case. The information is documented in (Tables 1 and 2). The alpha-amylase inhibition of ethanolic extracts is higher in both extracts and comparable to the standard, given by bar graphs (Figures 1 and 2).

Table 1 Alpha-amylase inhibitory activity of *Musa paradisiaca* L (AB)

STANDARD		PET.ETHER	CHLOROFORM	ETHANOL	WATER
Conc. µl	% alpha-amylase inhibition	% alpha-amylase inhibition	% alpha-amylase inhibition	% alpha-amylase inhibition	% alpha-amylase inhibition
Control	0.87				
100	40.23	6.89	9.31	32.18	18.27
200	43.68	11.72	18.16	40.22	21.03
300	49.42	17.93	20.34	44.83	29.88
400	56.32	21.03	29.77	58.62	31.84

Table 2 Alpha-amylase inhibitory activity of *Mangifera indica* L

STANDARD		PET.ETHER	CHLOROFORM	ETHANOL	WATER
Conc. µl	% alpha-amylase inhibition	% alpha-amylase inhibition	% alpha-amylase inhibition	% alpha-amylase inhibition	% alpha-amylase inhibition
Control	0.87				
100	40.23	4.59	10.34	21.84	16.55
200	43.68	9.08	16..89	28.73	19.19
300	49.42	15.63	18.1	36.78	21.37
400	56.32	19.65	27.12	39.08	29.65

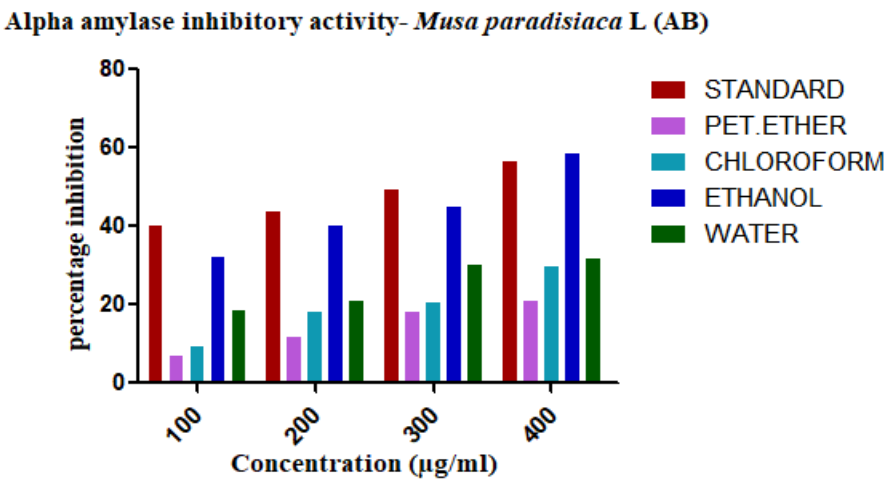

Figure 1 Alpha-amylase inhibitory activity of *Musa paradisiaca* L (AB)

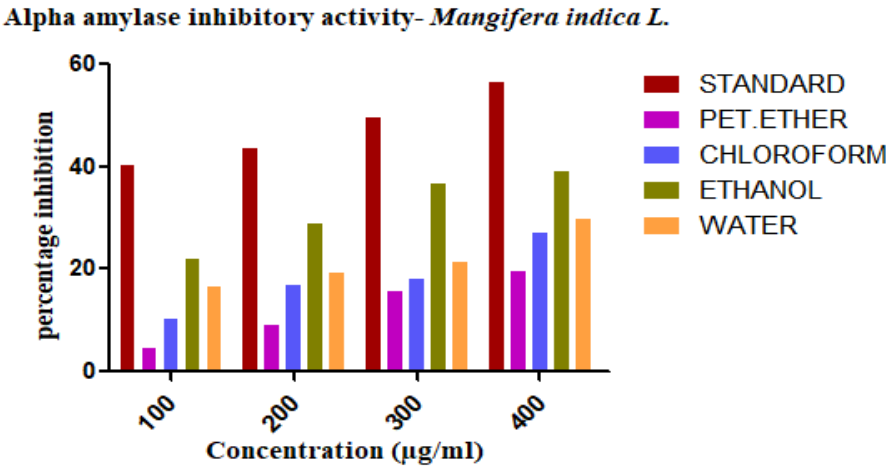

Figure 2 Alpha-amylase inhibitory activity of *Mangifera indica* L

Alpha-glucosidase inhibition assay

It determines a substance's antidiabetic potential by assessing its ability to inhibit the enzyme alpha-glucosidase, which is responsible for releasing glucose from carbohydrates. In this assay, the sample and the standard (acarbose) were tested and the percentage of alpha-amylase inhibition was calculated for all the extracts of *Musa paradisiaca* L. (AB) and *Mangifera indica* L. Absorbance was measured at 540 nm using a spectrophotometer. The results, documented in Tables 3 and 4, show that the ethanolic extracts of both plants exhibit a higher percentage of alpha-amylase inhibition, closely resembling the effect of the standard, as illustrated in bar graphs (Figures 3 and 4).

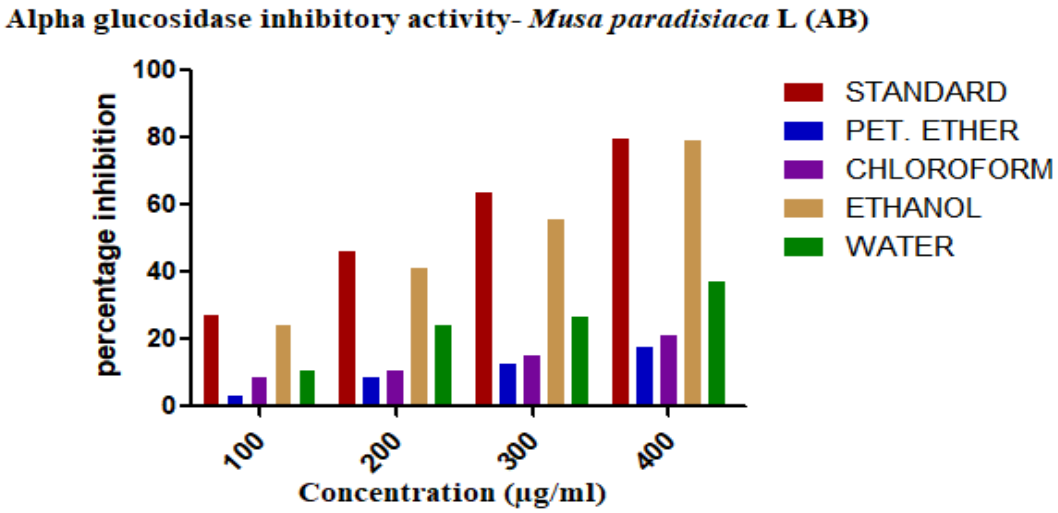

Figure 3 Alpha-glucosidase inhibitory activity of *Musa paradisiaca* L (AB)

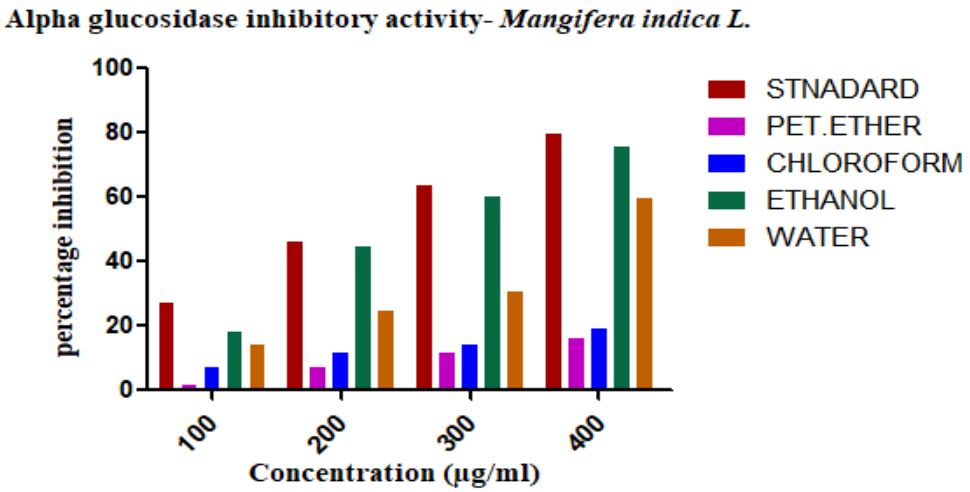

Figure 4 Alpha-glucosidase inhibitory activity of *Mangifera indica* L

Table 3 Alpha-glucosidase inhibitory activity of *Musa paradisiaca* L (AB)

STANDARD		PET.ETHER	CHLOROFORM	ETHANOL	WATER
Conc. µl	% alpha-glucosidase inhibition	% alpha-glucosidase inhibition	% alpha-glucosidase inhibition	% alpha-glucosidase inhibition	% alpha-glucosidase inhibition
Control	0.87				
100	26.86	2.98	8.80	23.88	10.74
200	46.11	8.65	10.74	40.89	24.18
300	63.58	12.38	14.92	55.52	26.42
400	79.40	17.61	21.19	78.95	37.01

Table 4 Alpha-glucosidase inhibitory activity of *Mangifera indica* L

STANDARD		PET.ETHER	CHLOROFORM	ETHANOL	WATER
Conc. µl	% alpha-glucosidase inhibition	% alpha-glucosidase inhibition	% alpha-glucosidase inhibition	% alpha-glucosidase inhibition	% alpha-glucosidase inhibition
Control	0.87				
100	26.86	1.58	7.31	17.91	14.02
200	46.11	7.16	11.49	44.47	24.77
300	63.58	11.791	14.32	60.15	30.74
400	79.40	15.97	18.95	75.67	59.55

***In-vivo* antidiabetic activity**

In-vitro antidiabetic assays indicated that the ethanolic extracts exhibited the highest activity levels among the extracts tested highlighting its potential therapeutic value. Hence for *in-vivo* antidiabetic activity, we have proceeded with the ethanolic extracts.

Toxicity studies

Doses were administered increasingly following OECD guidelines 423. Toxicity was observed at doses above 600 mg/kg, leading to 60 mg/kg (low dose) and 120 mg/kg (high dose) being selected for further study. The doses were fixed at ratios 1/10th and 1/5th.

Evaluation parameters

Effect of Musa paradisiaca L (AB) and Mangifera indica L ethanolic extracts on blood glucose level in streptozotocin-nicotinamide-induced diabetic rats

Compared to normal control rats, diabetic control rats had noticeably higher blood glucose levels. Diabetic rats treated with glibenclamide (10 mg/kg) and nicotinamide (20mg/kg), high doses of *Musa paradisiaca* L. (AB) ethanolic extract (MPET) and *Mangifera indica* L ethanolic extract (MIET) (120mg/kg) showed a significant decrease ($p < 0.001$) in blood glucose levels when compared to diabetic control rats. Diabetic rats treated with low doses of MPET and MIET (60 mg/kg) showed a less significant reduction in blood glucose levels when compared to the diabetic control group. The effect of MPET and MIET on the blood glucose level of male albino Wistar rats is given in Table 4a and depicted in the graph (Figure 5).

Table 4a Effect of MPET and MIET in blood glucose level for male albino Wistar rats

Blood Glucose level (mg/dL)				
GROUPS	0th DAY	7th DAY	14th DAY	21st DAY
Normal Control	113.5±3.052	115.5±2.837	116.6±2.564	118±0.683
Diabetic Control	502±3.530	509.5±0.991	512.1±1.275	513.8±1.351
Standard Glibenclamide+ Nicotinamide(10mg/kg+20mg/kg)	503.6±0.881	298.6±1.282	225±1.591	167±3.678
Low Dose of MPET (60 mg/kg)	500.1±2.468	352.5±1.765	275.1±1.275	223.7±0.872
High Dose of MPET (120mg/kg)	503.8±1.013	294.6±0.666	225.8±1.249	163.8±0.872
Low Dose of MIET (60 mg/kg)	505.3±1.520	317. 3±0.918	238.5±1.258	181±1.527
High Dose of MIET (120mg/kg)	507.6±0.843	306±0.966	229.1±0.600	172.3±1.763

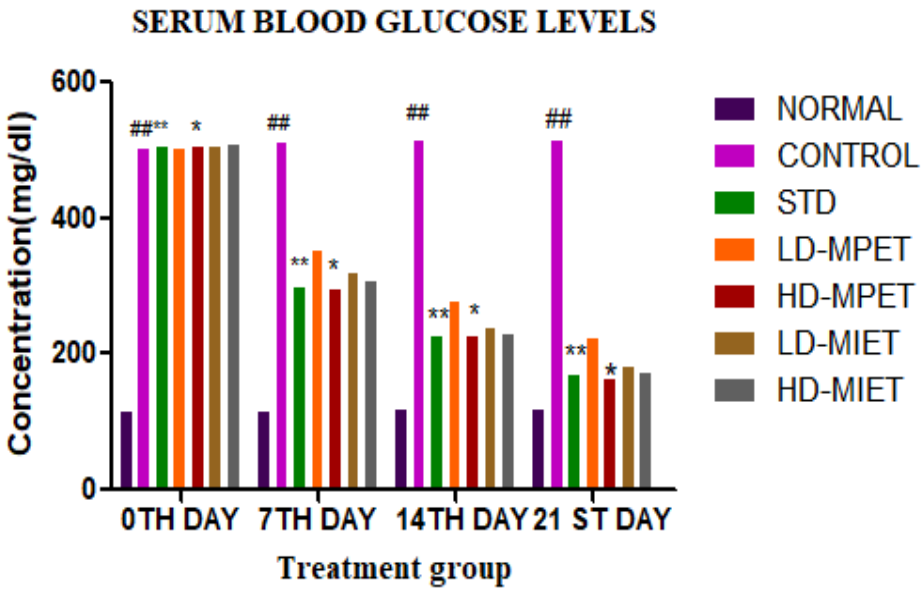

Figure 5 Comparison for serum blood glucose levels

Effect of Musa paradisiaca L (AB) and Mangifera indica L ethanolic extracts on body weight in Streptozotocin-Nicotinamide induced diabetic rats

Table 5 and Figure 6 present data on the body weight progression of seven groups of male albinos Wistar rats over 21 days, each group subjected to different treatments in a study of diabetes management. The Normal Control group shows a steady increase in weight, serving as a baseline for healthy growth. In contrast, the Diabetic Control group exhibits a consistent decline in body weight, reflecting the adverse effects of diabetes. The Standard Treatment group, receiving Glibenclamide and Nicotinamide, gains weight similarly to the Normal Control, indicating the treatment's effectiveness.

Table 5 Effect of MPET and MIET in body weight for male albino Wistar rats

Body weight (grams)				
GROUPS	**0th DAY**	**7th DAY**	**14th DAY**	**21st DAY**
Normal Control	238.6±0.918	250.6±0.643	269.6±1.791	284.1±1.249
Diabetic Control	254.5±1.543	227±1.164	198.6±1.109	177.3±1.115
Standard Glibenclamide+ Nicotinamide (10mg/kg+20mg/kg)	252±0.653	230.5±2.247	241.5±1.821	255.6±0.881
Low Dose of MPET (60 mg/kg)	241.3±1.642	216.5±0.784	219.1±2.013	248.8±0.77
High Dose of MPET (120 mg/kg)	253.5±0.763	232.33±1.938	238.5±0.991	244.1±1.006
Low Dose of MIET (60 mg/kg)	251.1±1.18	229.6±1.855	235.1±0.40	240±1.983
High Dose of MIET (120mg/kg)	251.3±2.060	227.8±1.2009	230.3±1.063	236.6±1.21

Both Low Dose (60 mg/kg) and High Dose (120 mg/kg) of MPET show progressive weight gain, with the high dose yielding a more substantial increase, suggesting a dose-dependent effect of the Methanolic Plant Extract Treatment. The Low Dose (60 mg/kg) and High Dose (120 mg/kg) of MIET also lead to weight gain, with the high dose of MIET showing comparable results to the high dose of MPET. This trend indicates that both MPET and MIET, particularly at higher doses, effectively mitigate diabetes-induced weight loss in rats.

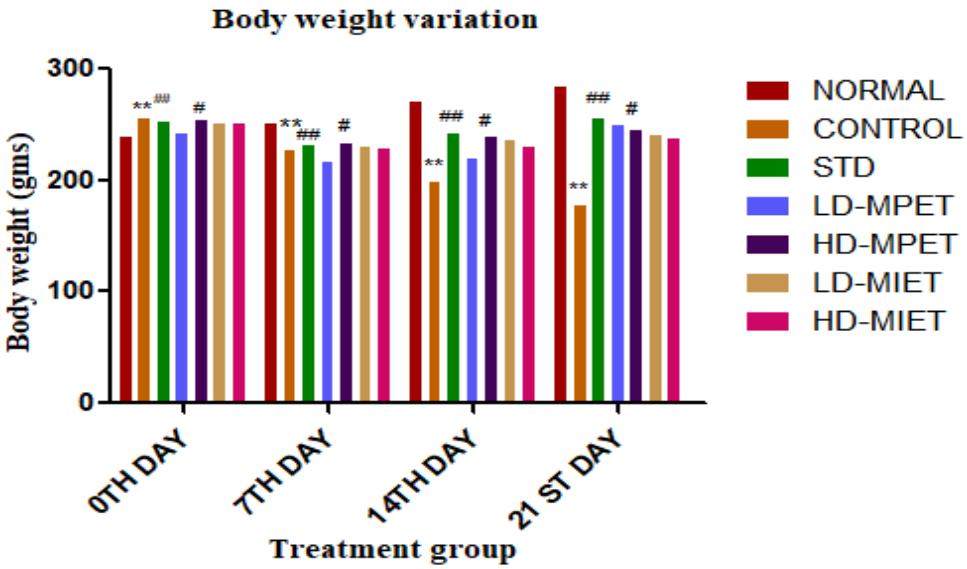

Figure 6 Comparison of body weight variation

Effect of Musa paradisiaca L(AB) and Mangifera indica L. on serum biochemical parameters of Streptozotocin-Nicotinamide induced diabetic rats

Table 6 and Figures 7-10 display the effects of different treatments on the lipid profile of male albino Wistar rats, measuring total cholesterol, triglycerides, LDL, and HDL levels. Standard Control rats have low cholesterol and triglycerides with balanced LDL and HDL levels. Diabetic Control rats show significantly higher cholesterol, triglycerides, and LDL, and reduced HDL, indicating disrupted lipid metabolism. Standard Treatment (Glibenclamide + Nicotinamide) results in near-regular lipid levels, suggesting treatment efficacy. Both Low and High Doses of MPET (60 mg/kg and 120 mg/kg) lower lipid levels, with the high dose showing better lipid regulation. Similarly, Low and High Doses of MIET improve lipid profiles, but the high dose more effectively reduces cholesterol and LDL.

Table 6 Effect of MPET and MIET on serum biochemical parameters for male albino Wistar rats

Lipid profile (mg/dl)				
GROUPS	**Total Cholesterol**	**Triglycerides**	**LDL**	**HDL**
Normal Control	131.4±0.31	77.6±2.121	38.5±0.651	49.7±0.954
Diabetic Control	267.9±0.98	148.4±1.78	69.7±1.719	29.3±0.118
Standard Glibenclamide+ Nicotinamide (10mg/kg+20mg/kg)	144±0.177	84.3±0.799	38.4±1.911	51.0±1.073
Low Dose of MPET (60 mg/Kg)	263.1±0.901	139.6±0.751	51.6±0.260	39.6±0.450
High Dose of MPET (120 mg/Kg)	163.4±1.867	97.7±0.745	42.8±0.382	43.9±0.667
Low Dose of MIET (60mg/kg)	227.7±0.123	128.5±1.223	50.3± 0.519	35.2±0.519
High Dose of MIET (120mg/kg)	178±0.886	103.8±0.237	46.1±0.443	39.1±1.847

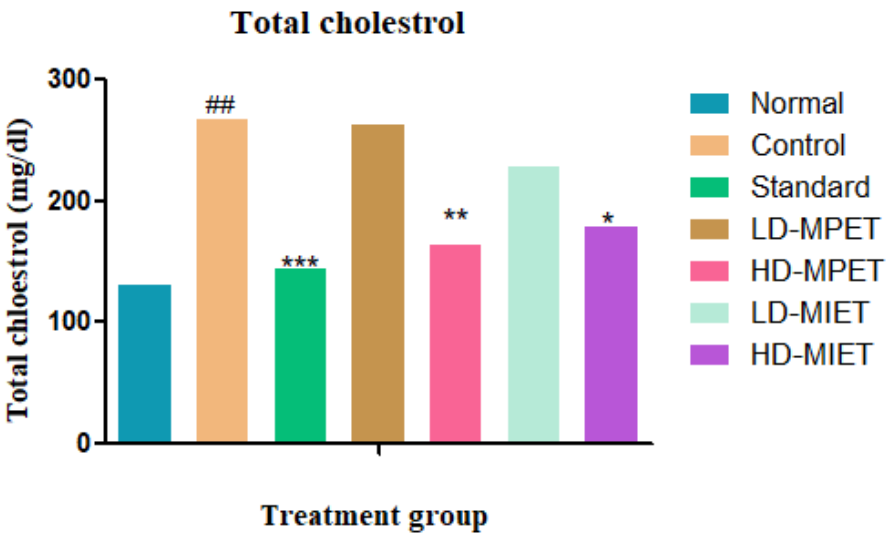

Figure 7 Variation of total cholesterol

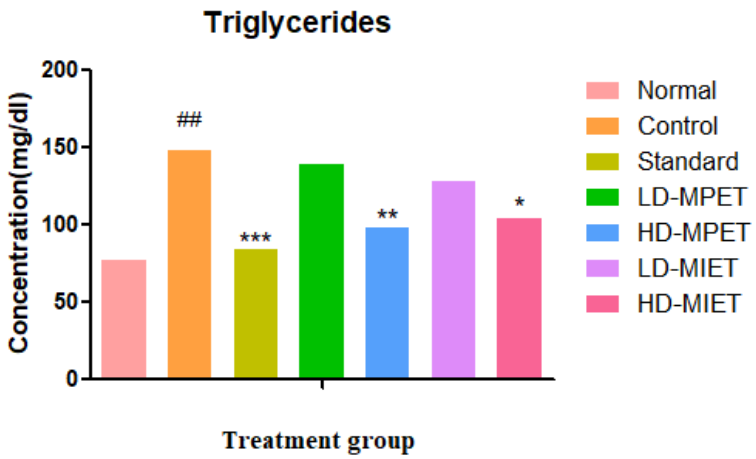

Figure 8 Variation in serum Triglycerides

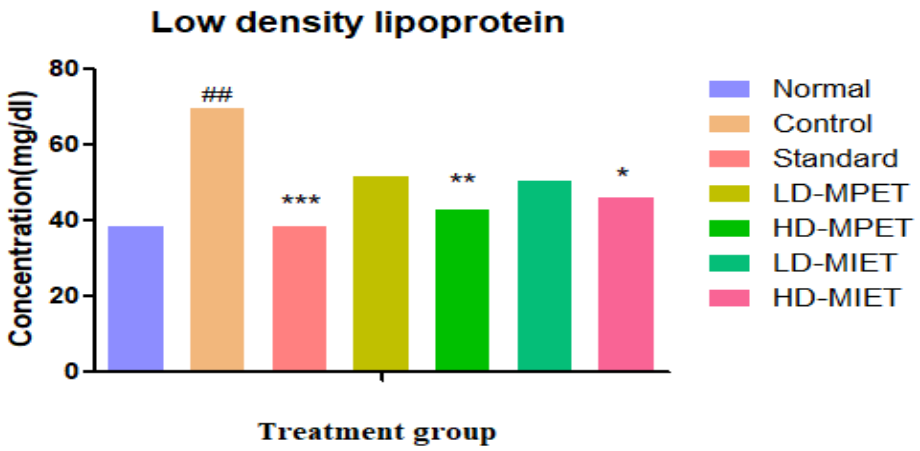

Figure 9 Variation of serum LDL levels

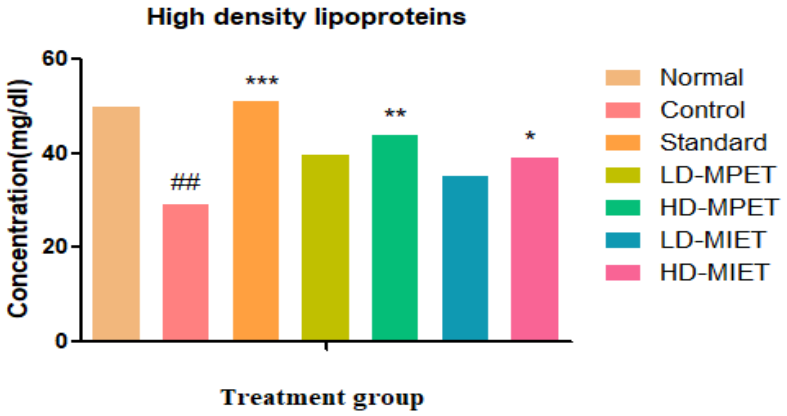

Figure 10 Variation of serum HDL levels

Histopathological examination of rat Pancreas

Normal control: The Islets of Langerhans are well-defined, rounded, oval-shaped structures with obvious borders that are distributed throughout the pancreas. The exocrine portion of the pancreas is primarily made up of acinar cells. There is little interstitial tissue, and the collagen fibres and fibroblasts are few. The pancreatic portion exhibits a healthy blood supply, with tiny veins and capillaries, particularly in the islets, clearly evident (Figure 11A).

Diabetic control: The number and size of the Islets seem to have significantly decreased. Some beta cells exhibit shrinkage or degeneration, while the few left exhibit injury or necrosis. Hypertrophy of acinar cells is seen. The existence of invading inflammatory cells, such as macrophages and lymphocytes, verifies inflammation. Blood vessel density and visibility are decreased, and collagen and extracellular matrix are deposited in the pancreatic interstitial spaces (Figure 11B).

Standard: Comparing the Islets of Langerhans to untreated diabetic rats, histopathological analysis shows numerous populations of beta cells. The recovery of beta cells that produce insulin may be indicated by the enhanced structure and more regular and defined look of the islets. Inflammatory indicators, such as macrophages and lymphocytes, are declining. Vascularization is more normalized, displaying better blood vessel density and structure, while acinar cells have improved form and function (Figure 11C).

Low dose of Musa paradisiaca L (AB): There are indications of atrophy in the beta cells. There are discernible secondary alterations in acinar cells, with comparatively fewer lymphocytes. There are blood vessels again (Figure 11D).

High dose of Musa paradisiaca L (AB): The size, shape, and distribution of the Islets of Langerhans are more regular. With the population of insulin-producing cells restored or almost regular, the previously injured beta cells show indications of recovery. The Islets recover their distinctive oval form and limits. The inflammatory response may have diminished if inflammatory cells such as macrophages and lymphocytes are absent. There is no fibrosis or scarring, and the acini seem delineated and not significantly atrophying. There is a sufficient quantity of blood (Figure 11E).

Low dose of Mangifera indica L: There are slight indications of atrophy, and the islets seem regular. Fibrovascular septa divide pancreatic tissues, and inflammation is significantly decreased. The pancreas exhibits a high blood vessel density and comprises intact acinar cells with intralobular ducts (Figure 11F).

High dose of Mangifera indica L: The size of the beta cells has grown, indicating a promising recovery. The extracellular matrix volume is decreased, and the islets appear oval-shaped and evenly dispersed. Signs of hypertrophy have decreased, and acinar cells seem in good health. There are plenty of vascular capillaries in the tissue (Figure 11G).

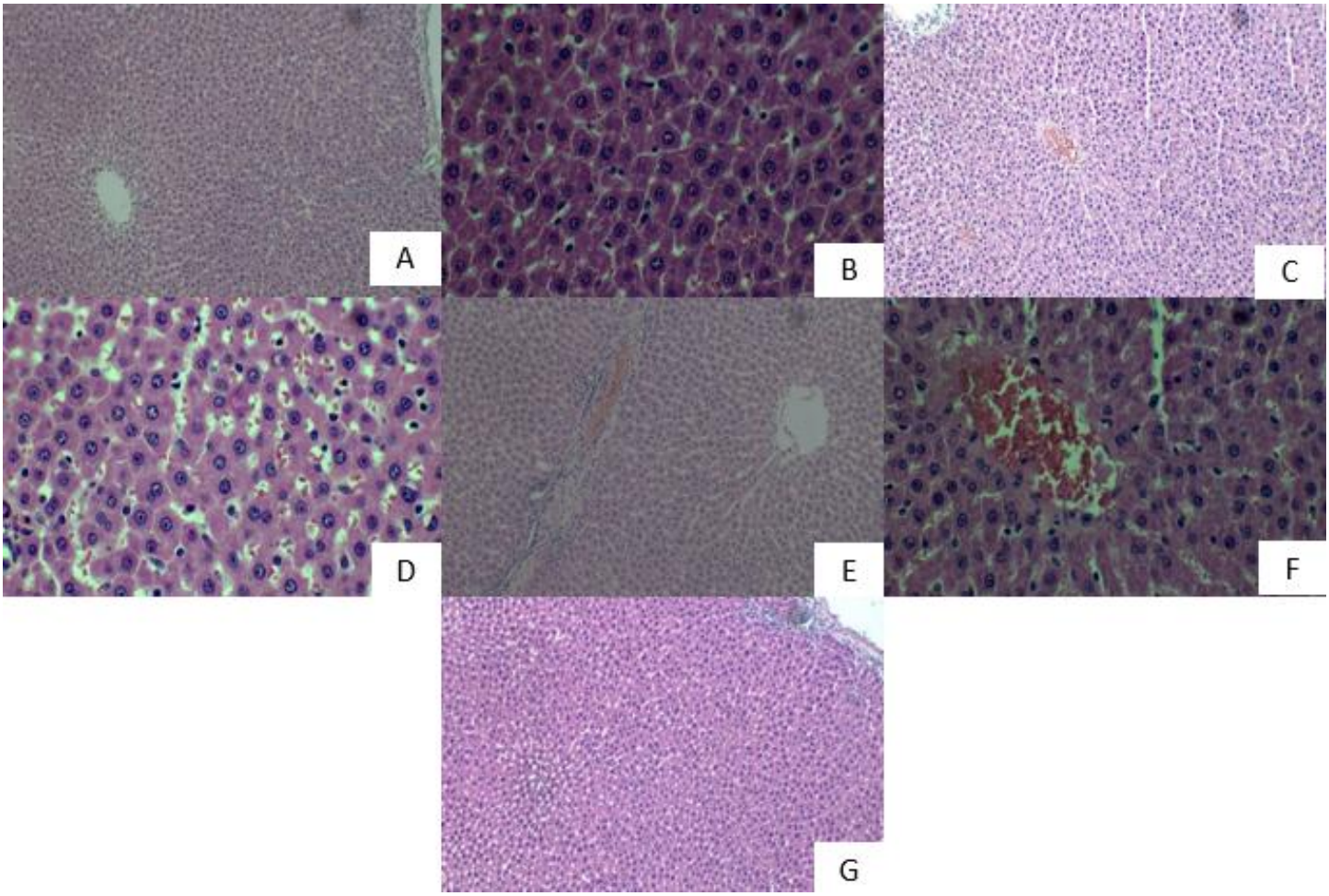

Figure 11 Histopathological evaluation of rat pancreas

Histopathological evaluation of rat Liver

Normal: The liver shows a distinct lobular structure, including central veins, portal regions, and hepatic cords. Hepatocytes exhibit a typical polygonal form with centrally positioned nuclei. Vascular spaces are visible, lined by endothelial cells (Figure 12A).

Diabetic control: Degeneration, cell death, and apoptosis are apparent in the liver cells. The presence of inflammatory cells indicates active inflammation or an immune response. Fibrosis and scarring point to chronic liver damage, with irregularities in liver sinusoids and central veins (Figure 12B).

Standard: Damaged liver cells exhibit signs of recovery, with a noticeable decrease in inflammatory cells within the liver tissue. Glycogen storage is restored in hepatocytes, with minimal signs of fatty liver or lipid changes. There is no evidence of fibrosis (Figure 12C). The liver parenchyma shows moderate recovery, with some improvement in previously distorted hepatocytes and sinusoids. Inflammatory cells persist, and the vascular lining is less pronounced (Figure 12D).

Low Musa paradisiaca L (AB) dose: The hepatocyte structure appears regular, with signs of regeneration and minimal or no inflammation. Glycogen levels have returned to regular compared to controls, lipid content remains stable, and there is no indication of fatty liver changes. Fibrosis or scarring is absent, and the vascular lining is well-defined (Figure 12E).

Low dose of Mangifera indica L: High dose of *Musa paradisiaca* L (AB): This liver tissue section displays intact hepatocytes and sinusoids, with moderate chronic inflammation around the periportal area and mild vacuolation in hepatocytes. The vascular supply is good, with minimal evidence of fibrosis (Figure 12F).

High dose of Mangifera indica L: Cell structure shows improvement, with reduced signs of necrosis and apoptosis. Inflammatory cell infiltration has lessened, suggesting a decrease in inflammation. Traces of glycogen indicate metabolic recovery, with minimal signs of scarring or tissue repair (Figure 12G).

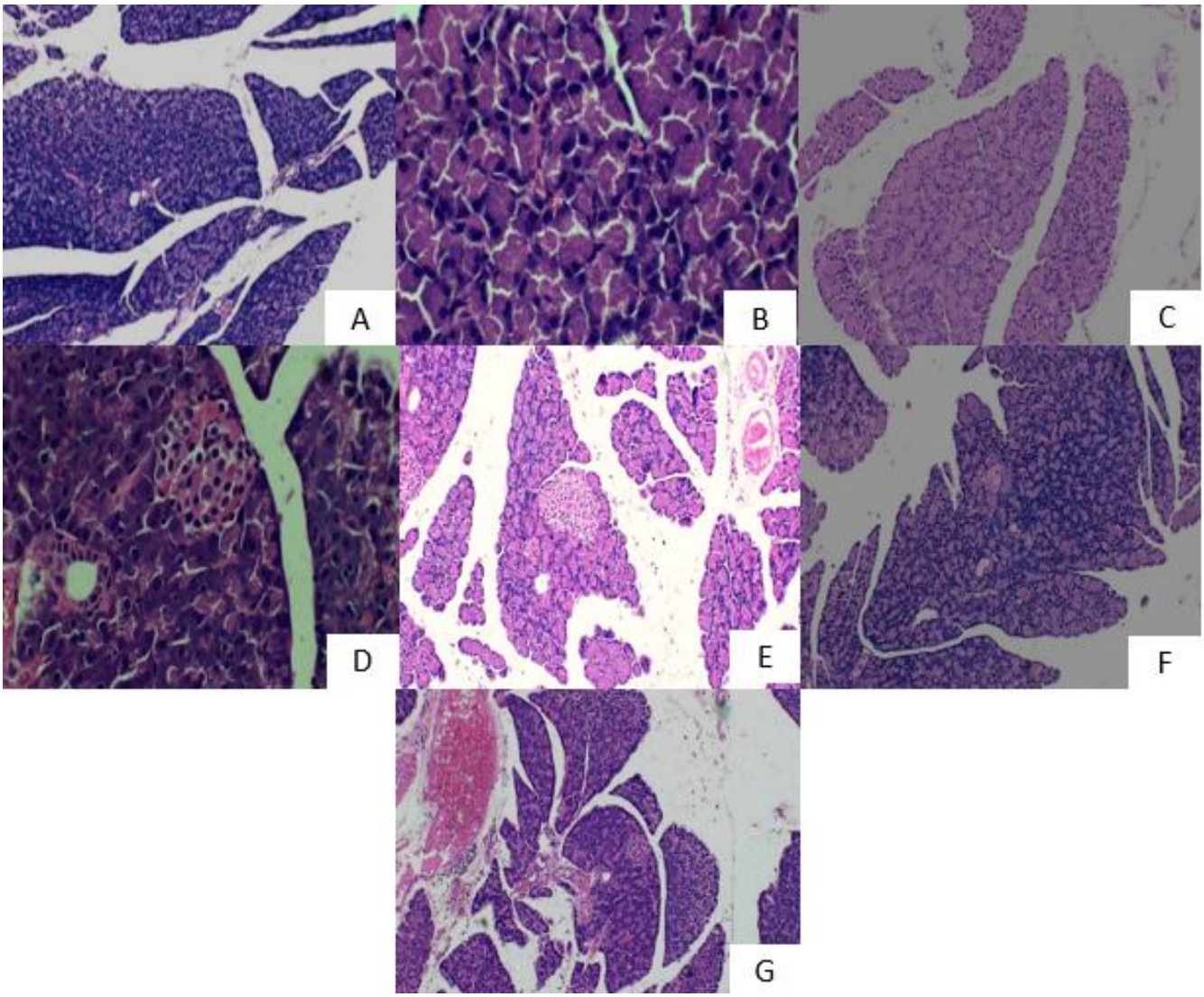

Figure 12 Histopathological evaluation of rat Liver

Enzyme inhibition assays revealed strong antidiabetic potential in both *Musa paradisiaca* L (AB) and *Mangifera indica* L, with *Musa paradisiaca* L (AB), especially in its ethanolic extract, showing more significant alpha-amylase and alpha-glucosidase inhibition. This suggests its bioactive compounds may be particularly effective in slowing carbohydrate breakdown and managing blood glucose, with effects comparable to the standard drug acarbose. In diabetic rats, *Musa paradisiaca* L (AB) and *Mangifera indica* L both reduced blood glucose, with *Musa paradisiaca* L (AB) showing a more potent effect. At a 120 mg/kg dose, *Musa paradisiaca* L (AB) lowered glucose from 503.8 mg/dL to 163.8 mg/dL over 21 days, outperforming *Mangifera indica* L, which reduced it from 507.6 mg/dL to 172.3 mg/dL. *Musa paradisiaca* L (AB) improved body weight and serum lipids more effectively. At the same time, histopathological studies showed better pancreatic and liver recovery, likely due to its higher levels of bioactive polyphenols and flavonoids.

4. CONCLUSION

The findings demonstrate that ethanolic extracts of *Musa paradisiaca* L. (AB) and *Mangifera indica* L. inflorescences exhibit strong anti-diabetic properties. Both plants effectively reduced blood glucose levels, improved lipid profiles, and contributed to tissue recovery in diabetic rat models, highlighting their potential as complementary therapies for managing diabetes mellitus.

Ethical approval & Declaration

This study was approved by the appropriate institutional animal ethical committee (AACP/IAEC/42/FEB2024/03) Al-Ameen College of Pharmacy, Bengaluru and certify that the study was performed per the ethical standards. Meantime, the ethical guidelines for plants & plant materials are also followed in the study for plant collection, identification & experimentation.

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Author's Contributions

Silpa IS: Designing and implementation of the research, analysis of the results and writing the manuscript.
Akila E: Involved in planning, interpretation and supervision of the work.
Dr Krishna Murthy: Involved in the supervision of the work
Neha KB: Involved in the interpretation of work.
Kashifa Farheen: Contributed to the implementation of the research.

Informed consent

Not applicable

Conflicts of interests

The authors declare that there are no conflicts of interests.

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Data and materials availability

All data associated with this study are present in the paper.

REFERENCES

1. Alam U, Asghar O, Azmi S, Malik RA. General aspects of diabetes mellitus. Handb Clin Neurol 2014; 126:211-22. doi: 10 .1016/B978-0-444-53480-4.00015-1
2. Andrade-Cetto A, Becerra-Jiménez J, Cárdenas-Vázquez R. Alfa-glucosidase-inhibiting activity of some Mexican plants used in the treatment of type 2 diabetes. J Ethnopharmacol 2008; 116(1):27-32. doi: 10.1016/j.jep.2007.10.031

3. Banday MZ, Sameer AS, Nissar S. Pathophysiology of diabetes: An overview. Avicenna J Med 2020; 10:174-88.
4. Chandran R, Parimelazhagan T, Shanmugam S, Thankarajan S. Antidiabetic activity of Syzygium calophyllifolium in Streptozotocin-Nicotinamide induced Type-2 diabetic rats. Biomed Pharmacother 2016; 82:547-54. doi: 10.1016/j.biopha.2016.05.036
5. Heidari R, Zareae S, Heidarizadeh M. Extraction, Purification, and Inhibitory Effect of Alpha - Amylase Inhibitor from Wheat (Triticum aestivum Var. Zarrin). Pak J Nutr 2005; 4(2): 101-105. doi: 10.3923/pjn.2005.101.105
6. Hussain SZ, Naseer B, Qadri T, Fatima T, Bhat TA. Mango (*Mangifera indica*)—morphology, taxonomy, composition and health benefits. In: Fruits grown in highland regions of the Himalayas: Nutritional and health benefits. Springer International Publishing; 2021; 245-55. doi: 10.1007/978-3-030-75502-7_19
7. Jarald E, Joshi SB, Jain DC. Diabetes and herbal medicines. Iran J Pharm Ther (IJPT) 2008; 7(1):97-106.
8. Kalita P. An overview on *Mangifera indica*: Importance and its various pharmacological actions. Pharma Tutor 2014; 2(12):72-76.
9. Matsuura H, Asakawa C, Kurimoto M, Mizutani J. Alpha-glucosidase inhibitor from the seeds of balsam pear (Momordica charantia) and the fruit bodies of Grifola frondosa. Biosci Biotech Biochem 2002; 66:1576-8.
10. Parvez GM. Pharmacological activities of mango (*Mangifera indica*): A review. J Pharmacogn Phytochem 2016; 5(3):1-7.
11. Shaw JE, Sicree RA, Zimmet PZ. Global estimates of the prevalence of diabetes for 2010 and 2030. Diabetes Res Clin Pract 2010; 87(1):4-14. doi: 10.1016/j.diabres.2009.10.007
12. Shirwaikar A, Rajendran K, Punitha IS. Antidiabetic activity of alcoholic stem extract of Coscinium fenestratum in streptozotocin-nicotinamide induced type 2 diabetic rats. J Ethnopharmacol 2005; 97(2):369-74. doi: 10.1016/j.jep.2004.11.034
13. Singhal AK, Giri S, Kumar R. Investigation of in-vitro anti-oxidant & anti-ulcer activity of Angiogenesis latifolia Roxb (dhava). NeuroQuantology 2022; 20(11):5680-5686. doi: 10.14704/NQ.2022.20.11.NQ66568
14. Thalapaneni NR, Chidambaram KA, Ellappan T, Sabapati ML, Mandal SC. Inhibition of carbohydrate digestive enzyme by Talinum portulacifolium (Forssk) leaf extract. J Complement Integr Med 2008; 5:1-10.
15. Tharanathan RN, Yashoda HM, Prabha TN. Mango (*Mangifera indica* L.), "The king of fruits"—An overview. Food Rev Int 2006; 22(2):95-123. doi: 10.1080/87559120600574493