

In vitro and *in vivo* antidiabetic activity on leaves of *Merremia hederacea* (Burm. f.) Hallier f.

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ABSTRACT

Objective: *In vitro* antidiabetic activity of plant leaf extracts (petroleum ether, chloroform, ethyl acetate, and ethanol) of *Merremia hederacea* (Burm. f.) Hallier f. was investigated and also, *in vivo* antidiabetic activity of an active extract was evaluated against streptozotocin (STZ)-induced type 2 diabetes mellitus in rats. **Materials and Methods:** *In vitro* studies were performed using α -amylase and α -glucosidase enzyme inhibition assay. Based on the *in vitro* studies, the active ethanol extract was selected for the *in vivo* antidiabetic activity. STZ (60 mg/kg body weight [BW], i.p.) was used to induce type 2 diabetes mellitus in rats. The rats were divided into different groups and orally administered with active extract (200 and 400 mg/kg) and glibenclamide (5 mg/kg) for 21 days. Blood samples were collected from overnight fasted rats at 0, 7, 14, and 21 days of treatment and analyzed. **Results:** It was found that ethanol extract shows good antidiabetic activity compared to other extracts. At 320 μ g, ethanol extract shows greater percentage inhibition of 91.44% and 85.50% for alpha-amylase and alpha-glucosidase, respectively. The standard acarbose also shows greater percentage inhibition of 95.44%. Parameters such as BW changes, fasting blood glucose level, serum high-density lipoprotein (HDL), and low-density lipoprotein (LDL) were measured. On day 21, rats were sacrificed and pancreas was excised for the histopathological studies of pancreatic tissues. **Conclusion:** From the present study, it is evident that the ethanol extract on leaves of *M. hederacea* showed good α -amylase and α -glucosidase inhibition and also exerted a significant effect on lowering of blood glucose level against STZ-induced diabetic rats and significant reduction on serum LDL and significant increase serum HDL level. It suggests that the plant may have therapeutic value in diabetes and related complications.

Key words: Antidiabetic, glibenclamide, streptozotocin, *Merremia hederacea*

INTRODUCTION

Diabetes mellitus is a clinical syndrome characterized by inappropriate hyperglycemia caused by a relative or absolute deficiency of insulin or by a resistance to the action of insulin at the cellular level.^[1] It is the most common endocrine disorder, affecting 16 million individuals in the United States and as many as 200 million worldwide. Unhealthy lifestyle factors such as over eating, physical inactivity, and obesity can impair the body's ability to use insulin.^[2] This is called insulin resistance. The complications of diabetes mellitus include vascular disease (diabetic angiopathy), atherosclerosis, heart conditions and stroke, kidney disease (diabetic nephropathy), eye diseases, nerve damage (diabetic neuropathy), infections and wounds, cancer, musculoskeletal disorders,

and diabetic ketoacidosis.^[3] The symptoms of diabetes include excessive thirst (polydipsia), excessive urination (polyuria) and dehydration, and excessive hunger or appetite (polyphagia). Due to the undesired side effects of insulin and oral hypoglycemic agents, continuous efforts are being made to develop new compounds for the treatment of diabetes, especially from herbal origin which is safe and effective.^[4]

Merremia hederacea (Burm.f.) Hillier f., belongs to Convolvulaceae family, commonly known as Elikkatutalai,

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twinning or prostrate herb. *M. hederacea* can be used to treat colds, febrile disease, sunstroke, oliguria, tonsil inflammation, laryngitis, as well as leukorrhea. Leaves of *M. hederacea* can be used in the treatments of chapped hands and feet. The genus *Merremia* reports to contain phenolic compounds, flavonoids, sulfates, aliphatic pyrrolidine amides, tropane containing alkaloid, and the species possess to antioxidant, anti-inflammatory, and alpha-amylase inhibitory activity. However, to the best of our knowledge, no data are available for its used as antidiabetic. The present study was designed to evaluate the antidiabetic activity of this plant.^[5,6]

MATERIALS AND METHODS

Chemicals and Reagents

Accu-Chek active glucometer diagnostics kit and glucose oxidase-peroxidase reactive strips (Accu-Chek Roche Diagnostics, USA) were used for the estimation of fasting blood glucose. Streptozotocin (STZ) was bought from Sigma Co. (USA). Glibenclamide was obtained from Sanofi India Ltd., Mumbai. All solvents used in this study were of analytical reagent grade.

Collection of Plant Material

The leaves of *M. hederacea* were collected in the Tirunelveli district, Tamil Nadu, India. It was authenticated by Dr. V. Chelladurai, Govt. Research Officer, Botany C.C.R.A.S., Govt. of India, (Retired), Tirunelveli. Herbarium specimen was prepared as per standard methods.

Preparation of Extracts

Fresh plant leaves were shade dried at room temperature, ground into coarse powder, and stored in airtight containers. The dried powder of leaves was extracted sequentially by hot continuous percolation method by Soxhlet apparatus using petroleum ether, chloroform, ethyl acetate, and ethanol as solvent. The extracts were concentrated using a rotary vacuum evaporator.

Phytochemical Screening of Extracts from *M. hederacea*

All the extracts were subjected to preliminary phytochemical screening for the detection of various plant constituents present. The pharmacological actions of crude drugs were determined by the nature of their constituents and the phytoconstituents are responsible for the desired therapeutic properties.^[7,8]

In vitro Antidiabetic Activity

All the four extracts were subjected to *in vitro* antidiabetic activity by alpha-amylase and alpha-glucosidase inhibition assay.

Procedure

Alpha-amylase inhibitory activity

This study was performed by a modified starch iodine protocol. In short, plant extracts and standard concentration (10, 20, 40, 80, 160, and 320 µg/mL) was taken in pre-labeled test tubes. A volume of 20 mL of α-amylase was added to each test tube and incubated for 10 min at 37°C. After the incubation, 200 µL of 1% starch solution was added to each test tube and the mixture was reincubated for 1 h at 37°C. Then, 200 µL of 1% iodine solution was added to each test tube and after that, 5 mL distilled water was added. Absorbance of the mixture was taken at 565 nm. Blank was undertaken under the same conditions. IC₅₀ value was calculated using regression analysis.^[9]

$$\%inhibition = \frac{As - Ac}{As} \times 100$$

Where, *Ac* is the absorbance of the control and *As* is the absorbance of the sample.

Alpha-glucosidase inhibition assay

The effect of the plant extracts on α-glucosidase activity was determined using α-glucosidase enzyme. The substrate solution of p-nitrophenyl glucopyranoside (pNPG) was prepared in 20 mM phosphate buffer and pH 6.9. 100 µL of α-glucosidase was pre-incubated with 2.5 ml of the different concentrations of the extracts for 10 min. Then, 50 µL of 3.0 mM (pNPG) as a substrate dissolved in 20 mM phosphate buffer (pH 6.9) was then added to start the reaction. The reaction mixture was incubated at 37°C for 20 min and stopped by adding 0.5 mL of Na₂CO₃ (0.1 M). The yellow-colored reaction mixture, 4-nitrophenol, released from pNPG was measured at 405 nm using ultraviolet-visible spectrophotometer. Acarbose was used as a positive control and the inhibitory activity of α-glucosidase was calculated using the following formula.^[10]

$$\% \text{ Inhibition} = \left(\frac{[\text{Abs Control} - \text{Abs Sample}]}{\text{Abs Control}} \right) \times 100.$$

In vivo Antidiabetic Activity

Acclimatization of animals

Animals of either sex of Wistar rats (7–8 week; 150–190 g), maintained in sanitized polypropylene cages (6%) in air-conditioned rooms (23 ± 2°C, 35–60% humidity with 12 h light-dark cycle), were obtained from Animal House, Madras Medical College. The rats were fed with pellet diet and water *ad libitum*. Prior approval was obtained from the Institutional Animal Ethical Committee (1917/ReBi/S/16/CPCSEA/25.10.2016). They were maintained in controlled laboratory conditions of 12 h dark/light cycle, 22 ± 2°C temperatures, and 45–60% humidity.

Experimental design

Animals were divided into five groups of six rats each.

- Group 1 (Normal control) – Normal saline (1 ml/kg/day, p.o.)
- Group 2 (Diabetic control) – STZ + 1% Carboxymethylcellulose (CMC) (1 ml/kg/day, p.o.)
- Group 3 (Positive control) – STZ + Glibenclamide (5 mg/kg/day, p.o.) for 21 days
- Group 4 (Low dose) – STZ + Ethanolic extract of *M. hederacea* (ETMH) (200 mg/kg/day, p.o.) for 21 days
- Group 5 (High dose) – STZ + ETMH (400 mg/kg/day, p.o.) for 21 days.

The test drug (*M. hederacea*) and the standard drug (glibenclamide) were administered orally as a suspension in 1% w/v CMC.

Preparation of 0.1 M citrate buffer

Accurately weighed quantity of trisodium citrate (1.49 g) was dissolved in sufficient Milli-Q water to produce 100 mL and was adjusted to pH 4.5 with HCl.

Preparation of STZ and nicotinamide solution

STZ is freely soluble in water and saline, but it is unstable in both. It is stable in 0.1 M citrate buffer. A solution of STZ of appropriate strength (depending on the required total dose per animal) was prepared by dissolving weighed quantity of STZ in freshly prepared ice-cold citrate buffer and was administered i.p. in volumes of ~2 mL/kg (dose: 60 mg/kg). STZ was freshly prepared because it is unstable. Nicotinamide was dissolved in normal saline to yield a strength that is appropriate for administration.

Experimental Induction of Diabetes

Diabetes was induced by STZ (60 mg/kg), 15 min after the intraperitoneal administration of nicotinamide (120 mg/kg). Diabetic rats were permitted to intake of 10% glucose solution overnight to overcome the initial drug-induced hypoglycemic death. After 72 h, the blood glucose was checked and the animals having a blood glucose level higher than 200 mg/dl were considered diabetic and used for the experiments.

Collection of Blood and Tissue Samples

After overnight fasting, the blood was withdrawn from the tail vein about 0.1 mL and fasting blood glucose level was checked using Accu-Chek glucometer on 0, 1, 7, 14, and 21 days period. Animal body weight (BW) is also recorded before and after the treatment. At the end of the 21st day experiment, rats were fasted overnight and blood samples were withdrawn through the retro-orbital plexus (2–5 mL) under light isoflurane anesthesia using a glass capillary tube and collected in a vacutainer blood collection tubes. Blood was allowed to clot and serum separated by centrifugation at 4000 rpm for 10 min.

Low-density lipoprotein (LDL) cholesterol and high-density lipoprotein (HDL) cholesterol were measured by enzymatic colorimetric methods using commercial kits.^[11] After the collection of blood samples, animal was sacrificed and pancreas was isolated for histopathological studies.

Histopathological Studies

At the end of the 21st day experiment, the selected rats were anesthetized by high dose of isoflurane and the animals were sacrificed and abdominally dissected. A portion of pancreatic tissue was dissected out and fixed in 10% buffered neutral formalin for 24 h. After fixation, the tissues were embedded in paraffin wax. About 5 microns thickness sections were prepared with microtome and mounted on clean glass slides and then they were deparaffinized in xylene twice for 5 min and then rehydrated with graded alcohol and stained with hematoxylin and eosin dye. The stained sections were examined and photographed using microscope.

Statistical Analysis

All the data are reported as mean \pm standard error of mean for six animals in each group. Statistical comparisons were determined by one-way analysis of variance followed by Dunnett's *t*-test.

RESULTS

Phytochemical Screening

From the preliminary phytochemical screening, it was observed that petroleum ether extract shows the presence of phytosterol, triterpenoids, proteins, amino acids, and fixed oils. Chloroform extract shows the presence of alkaloids, carbohydrates, phytosterol, flavonoids, proteins, and amino acids. Ethyl acetate extract shows the presence of glycosides, flavonoids, and terpenoids. Ethanolic extract shows the presence of glycosides, flavonoids, tannins, and phenolic compounds in extracts of *M. hederacea* [Table 1].

In vitro Studies

Alpha-amylase Assay

As illustrated in Table 2, alpha-amylase assay was carried out for the extracts of *M. hederacea*. It was found that ethanol extract shows good antidiabetic activity compared to other extracts. At the highest concentration of 320 μ g, ethanol extract shows greater percentage inhibition of 91.44%. The standard acarbose also shows good alpha-amylase inhibition with a percentage inhibition of 95.44%.

Alpha-Glucosidase Assay

As illustrated in Table 3, alpha-glucosidase assay was carried out for the extracts of *M. hederacea*. It was found that ethanol extract shows greater percentage inhibition of 85.50% at 320 µg. The standard acarbose also shows greater alpha-glucosidase inhibition with a percentage inhibition of 95.44.

Effect of Extract on Fasting Blood Glucose

Administration of STZ resulted in a significant ($P < 0.001$) increase in mean blood glucose level on days 1, 7, 14, and 21. Post-treatment with an ETMH in STZ-induced rats significantly reduces ($P < 0.001$) the increase of blood glucose level as compared to Group II. The administration

of ETMH produces dose-dependent effect as the high dose (400 mg/kg) shows more significant antidiabetic activity than 200 mg/kg. Treatment with glibenclamide after induction of diabetes significantly ($P < 0.001$) reduced the increased blood glucose level as compared to Group II [Table 4 and Figure 1].

Effect on BW

Table 5 and Figure 2 describe the changes in the BW of the control and experimental rats treated with ETMH and glibenclamide. The BW of the STZ-induced diabetic rats was lowered than that of the normal control groups at 7, 14, and 21 days. However, the administration of ETMH of 400 mg/kg significantly increases of the BW on 7, 14, and 21 days compared to standard glibenclamide.

Table 1: Preliminary phytochemical analysis on leaf extracts of *Merremia hederacea*

Test	Petroleum ether	Chloroform	Ethyl acetate	Ethanol
Alkaloids	-	+	-	+
Carbohydrates	-	+	-	-
Glycosides	-	-	+	+
Phytosterols	+	+	-	-
Flavonoids	-	+	+	+
Tannins and phenolic compounds	-	-	-	+
Proteins and amino acids	+	+	-	-
Saponins	-	-	-	+
Terpenoids	+	-	+	-
Fixed oils	+	-	-	-

+ Positive, -Negative

Table 2: Percentage inhibition of extracts of *Merremia hederacea* on alpha-amylase

Concentration in µg	Petroleum ether extract	Chloroform extract	Ethyl acetate extract	Ethanol extract	Acarbose (standard)
10	6.55	9.25	10.47	13.68	47.86
20	10.93	35.23	40.11	57.14	69.75
40	19.21	40.21	45.62	59.47	76.31
80	26.08	45.18	52.62	76.95	90.44
160	29.32	50.23	60.41	89.49	90.62
320	38.23	55.54	65.44	91.44	95.44

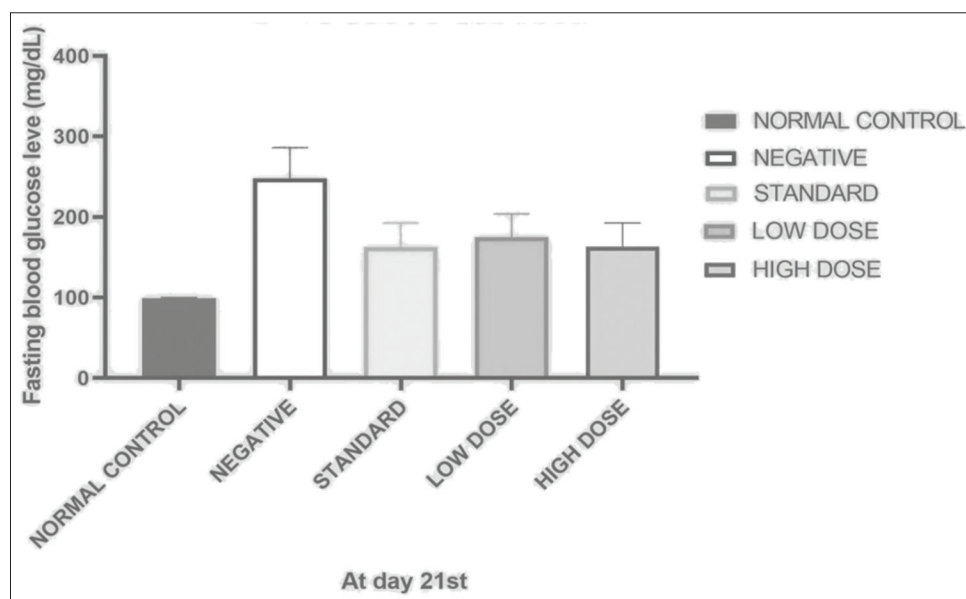
Table 3: Percentage inhibition of extracts of *Merremia hederacea* on alpha-glucosidase

Concentration in µg level	Petroleum ether extract	Chloroform extract	Ethyl acetate extract	Ethanol extract	Acarbose (standard)
10	3.15	4.33	3.15	19.24	47.86
20	6.72	9.94	8.93	22.12	69.75
40	23.86	25.21	19.81	40.27	76.31
80	31.82	34.01	27.94	55.27	90.44
160	72.96	71.40	59.38	78.58	90.62
320	62.24	70.33	69.82	85.50	95.44

Table 4: Effect of ETMH on fasting blood glucose level in STZ-induced diabetic rats

Treatment	Day 0	Day 1	Day 7	Day 14	Day 21
Normal control (saline)	98±2.42	99±2.12	100±2.03	103±1.76	99±2.21
Disease control (STZ induced)	100±2.82	275±4.33**	286±3.46	295±4.27	303±3.99**
Positive control STZ+Glibenclamide	102±1.41	212±3.86***	141±2.84**	119±2.95***	99±2.33***
STZ+extract low dose (200 mg/kg)	103±2.45	231±2.55***	160±2.18***	123±2.97***	106±2.85***
STZ+extract high dose (400 mg/kg)	105±1.64	209±3.70***	157±2.73***	123±1.65***	102±1.84***

All values are expressed as mean±standard error of mean. *** $P < 0.001$ versus Group III, significant by analysis of variance followed by Dunnett's *t*-test (at 200 and 400 mg/kg) (ETMH), positive control. ETMH: Ethanolic extract of *Merremia hederacea*, STZ: Streptozotocin

**Figure 1:** Effect of ethanolic extract of *Merremia hederacea* on fasting blood sugar level in streptozotocin-induced diabetic rats

Effect of LDL on STZ-induced diabetic rats

As illustrated in Table 6 and Figure 3, there was a significant rise ($P < 0.001$) in LDL level in STZ-induced diabetic rats when compared to normal group. The administration of glibenclamide has showed a significant ($P < 0.001$) lowering of LDL level at the 21st day. The administration of ETMH has showed a significant lowering ($P < 0.001$) of LDL level when compared to positive control.

Effect of HDL on STZ-induced diabetic rats

As illustrated in Table 6 and Figure 4, there was a significant decline ($P < 0.001$) in HDL level in STZ-induced diabetic rats when compared to normal group. The administration of glibenclamide has showed a significant ($P < 0.001$) increase of HDL level compared to Group II. The administration of ETMH at 400 mg/kg has showed a significant increase ($P < 0.001$) of HDL level on the 21st day when compared to positive control.

Histopathological Studies on Pancreas

STZ-induced diabetic rat pancreas

STZ-treated groups showing reduce islet of Langerhans. Low dose (200 mg/kg), high dose (400 mg/kg), and glibenclamide

(standard) treated groups showing recovery of islet of Langerhans. The number of islets cells was comparatively higher in 400 mg/kg than low dose 200 mg/kg. Hence, the number of islet cells increases in a dose-dependent manner [Figures 5-8].

DISCUSSION

The use of herbal drugs as complementary approaches in existing medications for the treatment of diabetes and its complications is growing worldwide and many plants in different countries are known to have antidiabetic effects.^[12] The ancient Indian literature reports more than 800 plants with antidiabetic properties while ethnopharmacological surveys indicate that more than 1200 plants can be used for hypoglycemic activity.^[13] Mainly two carbohydrate hydrolyzing enzymes (α -amylase and α -glucosidase) are responsible for postprandial hyperglycemia. α -amylase begins the process of carbohydrate digestion by hydrolysis of 1, 4-glycosidic linkages of polysaccharides (starch and glycogen) to disaccharides and α -glucosidase catalyzes the disaccharides to monosaccharides, which leads to postprandial hyperglycemia. Hence, inhibitors of α -amylase and α -glucosidase are useful in the control of hyperglycemia as

Table 5: Effect of ETMH on body weight in STZ-induced diabetic rats

Treatment	Day 0	Day 1	Day 7	Day 14	Day 21
Normal control (saline)	165±2.47	168±2.77	171±2.46	175±2.84	180±2.33
Disease control (STZ induced)	163±2.17	157±1.78	146±1.02	129±1.11	113±1.51**
Positive control STZ+glibenclamide	166±2.67	172±2.57	179±3.28	187±2.86	201±3.83***
STZ+extract low dose (200 mg/kg)	161±1.55	163±2.11	174±2.12	185±1.98	189±1.23**
STZ+extract high dose (400 mg/kg)	165±3.59	169±0.978	176±4.45	188±4.43	193±4.49***

All values are expressed as mean±standard error of mean. At 400 mg/kg (ETMH), ** $P < 0.001$ versus Group III, significant by analysis of variance followed by Dunnett's *t*-test. * $P < 0.05$, 400 mg/kg (ETMH). ETMH: Ethanolic extract of *Merremia hederacea*, STZ: Streptozotocin

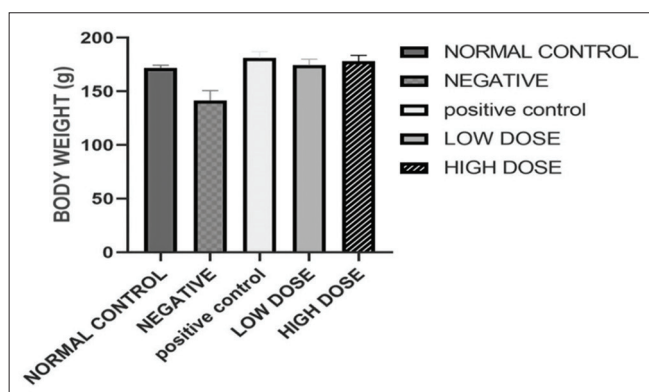


Figure 2: Effect of ethanolic extract of *Merremia hederacea* on body weight in streptozotocin-induced diabetic rats

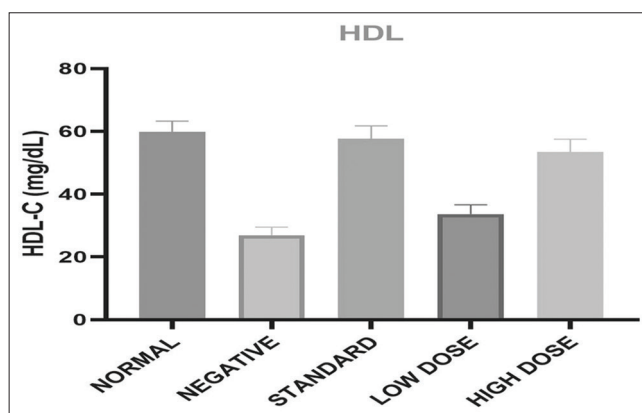


Figure 4: Effect of ethanolic extract of *Merremia hederacea* on high-density lipoprotein cholesterol in streptozotocin-induced diabetic rats on the 21st day

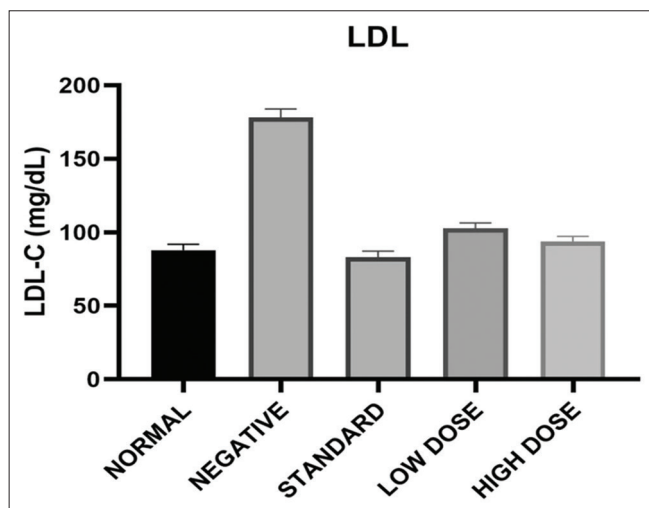


Figure 3: Effect of ethanolic extract of *Merremia hederacea* on LDL-C in streptozotocin-induced diabetic rats on the 21st day

they delay carbohydrate digestion, which consequently reduce the postprandial plasma glucose level.^[14,15]

Many bioactive compounds from different plants have been reported to have hypoglycemic effect, in that mostly phenolics, resin glycosides, and flavonoids have a positive correlation as antidiabetic agents.^[16] The ethanol extract shows greater percentage inhibition in both alpha-amylase and alpha-glucosidase compared to other extracts. The presence of flavonoids and phenolic compounds in ethanol extract of *M.*

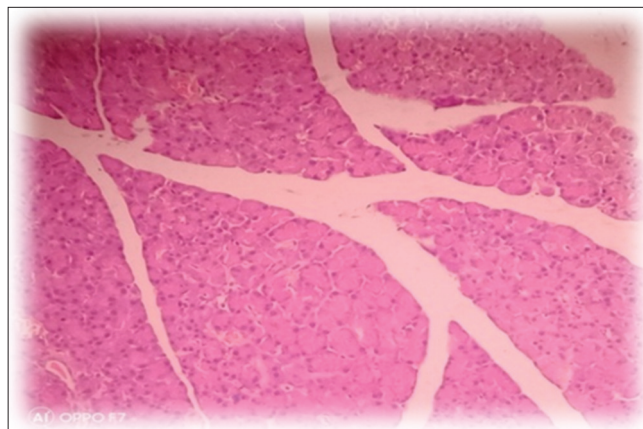


Figure 5: Streptozotocin-induced diabetic rat

hederacea may act against diabetes mellitus either through their capacity to avoid glucose absorption or to improve glucose tolerance by competitive inhibition of sodium-dependent glucose transporter-1. Another possible mechanism followed by flavonoid compounds (luteolin, kaempferol, chrysin, and galangin) to control blood glucose levels is the inhibition of α -amylase and α -glucosidase activity in the intestine.^[17,18]

The objective of treatment in diabetic patient is to lower blood glucose to normal level. In the present study, ETMH showed a significant lowering of blood glucose level, an index of diabetic control. STZ-induced diabetes is one of the widely used animal models that mimic the human diabetes

mellitus. In addition, STZ generates potential free radicals such as nitric oxide (NO) by intracellular metabolism of STZ and precipitate further β -cells DNA damage by strand break.

The concentration of blood glucose was significantly increased in STZ-induced diabetic as compared to normal control. Administration of ETMH (400 mg/kg) significantly reduced the raised blood glucose level in STZ-induced diabetic rats and the lowering was almost comparable to glibenclamide 5 mg/kg. Further, this antidiabetic activity of ETMH was associated with an increase in the serum insulin level revealed that ETMH may stimulate insulin secretion from regenerated β -cells and remaining β -cells. The blood glucose-lowering effect of the ETMH could be due to the presence of flavonoid and phenolic compounds as reported in the preliminary phytochemical screening. These findings were also supported by the previous experimental findings, wherein they reported the blood glucose-lowering effect of flavonoids.^[19,20]

The BW of the STZ-induced diabetic rats was lowered than that of the normal control groups at 7, 14 and 21 days. However, the administration of ETMH of 400 mg/kg significantly increases of the BW on 7, 14, 21 days compared to standard glibenclamide.

Table 6: Effect of ETMH on LDL-C and HDL-C in STZ-induced diabetic rats on the 21st day

Test	LDL-C	HDL-C
Normal control	88±1.68	60±1.40
Diabetic control STZ induced	178±2.39***	27±1.08**
Standard STZ+Glibenclamide	83±4.1.73***	58±1.67***
STZ+ETMH (200 mg/kg)	103±1.52**	34±1.20**
STZ+ETMH (400 mg/kg)	94±1.42***	54±1.65***

All values are expressed as mean±standard error of mean. At 400 mg/kg of ETMH, *** $P < 0.001$ versus Group II (STZ induced), significant by analysis of variance (ANOVA) followed by Dunnett's *t*-test. At 200 mg/kg of ETMH, ** $P < 0.01$ versus Group II (STZ induced), significant by ANOVA followed by Dunnett's *t*-test. ETMH: Ethanolic extract of *Merremia hederacea*, STZ: Streptozotocin, HDL-C: High-density lipoprotein cholesterol, LDL-C: Low-density lipoprotein cholesterol

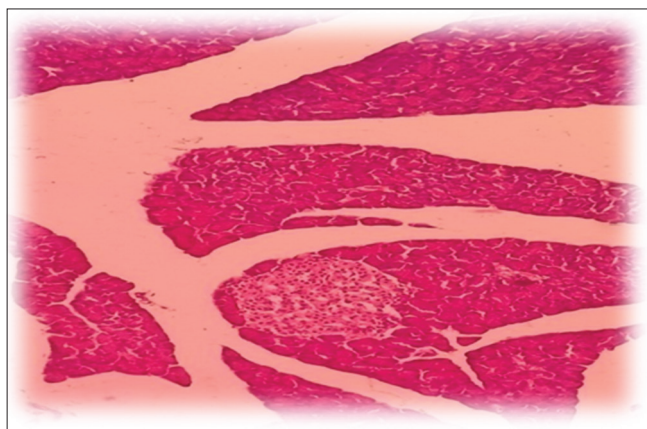


Figure 6: Standard (glibenclamide)

There was a significant rise ($P < 0.001$) in LDL level in STZ-induced diabetic rats when compared to normal group. The administration of glibenclamide has showed a significant ($P < 0.001$) lowering of LDL level at the 21st day. The administration of ETMH has showed a significant lowering ($P < 0.001$) of LDL level when compared to positive control.

Patients with type 2 diabetes show reduced turnover of their LDL particles with a reduction of catabolism, leading automatically to increased LDL plasma residence time. Augmented LDL residence time in plasma is likely to promote cholesterol deposition in the arterial wall.

There was a significant decline ($P < 0.001$) in HDL level in STZ-induced diabetic rats when compared to normal group. The administration of glibenclamide has showed a significant ($P < 0.001$) increase of HDL level compared to Group II. The administration of ETMH at 400 mg/kg has showed a significant increase ($P < 0.001$) of HDL level on the 21st day when compared to positive control.

Type 2 diabetes is associated with decreased plasma HDL cholesterol levels related to the reduction of the HDL 2

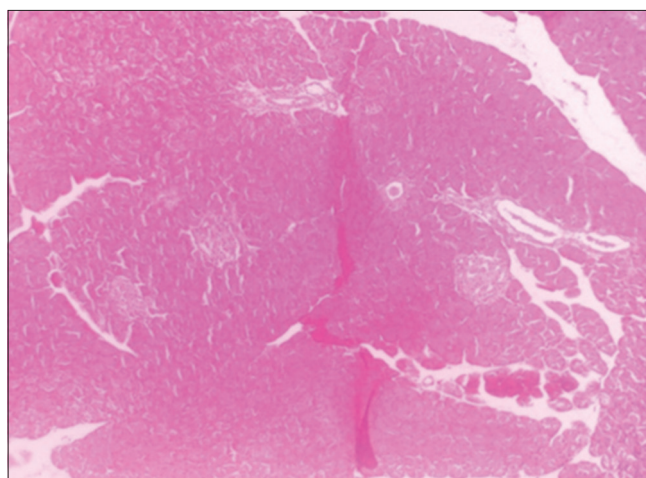


Figure 7: Ethanolic extract of *Merremia hederacea* (200 mg/kg)

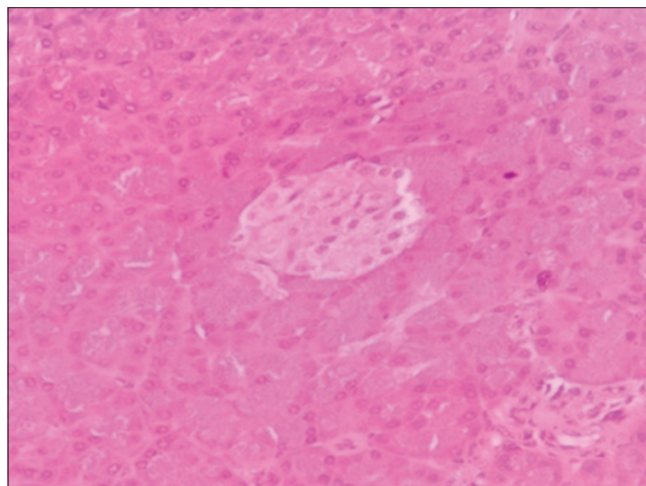


Figure 8: Ethanolic extract of *Merremia hederacea* (400 mg/kg)

subfraction. Reduced HDL 2 level, in type 2 diabetes, has been shown to be correlated with both hypertriglyceridemia and obesity. The decrease in HDL cholesterol, noted in patients with type 2 diabetes, is due to increased catabolism of HDL particles.^[21,22]

CONCLUSION

From the above discussion, it conclude that the ethanol extract possess good *in vitro* and *in vivo* antidiabetic activity. Ethanol extract of *Merremia hederacea* shows greater percentage inhibition than other extracts in both enzyme assay with 91.44% and 85.50% respectively at highest concentration. The ethanol extract effectively reversed the streptozotocin-induced changes in the blood sugar level and the beta-cell population in the pancreas.

The ethanol extract of *Merremia hederacea* at high dose (400 mg/kg) exhibited significant antidiabetic activity than at low dose (200 mg/kg) in streptozotocin-induced diabetic rats. The ethanol extract at 400 mg/kg also showed improvement in parameters like body weight and lipid profile as well as regeneration of cells of pancreas than at 200 mg/kg and might be of value in diabetes treatment. Further investigation is in necessary to determine the exact phytoconstituents (s) responsible for antidiabetic effect.

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