Vol 9|Issue 2| 2019 | 34-42.

e-ISSN 2248 - 9169
Print ISSN 2248 - 9150

International Journal of
Experimental Pharmacology

www.ijepjournal.com

ANTIDIABETIC, ANTIHYPERLIPIDAEMIC ACTIVITY OF METHANOLIC EXTRACT OF *LANTANA CAMARA* L LEAVES IN STREPTOZOTOCIN-INDUCED DIABETIC RATS

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ABSTRACT

The aim of the present study was to evaluate the antihyperglycemic and antihyperlipidemic activities of methanolic extract of *Lantana camara* Linn leaves (MELC) in streptozotocin (STZ) - induced diabetic rats. Diabetic rats were treated with oral administration of MELC (200 and 400 mg/kg) for 21 days. Various biochemical parameters such as serum glucose, plasma insulin, Glycosylated hemoglobin (HbA_1C), lipid profiles, and liver marker enzymes were measured to assess the antihyperglycemic and antihyperlipidemic activities of the extract. Administration of the MELC (200 mg/kg and 400 mg/kg) significantly decreased ($P < 0.05$; $P < 0.01$) blood glucose levels in diabetic rats and has the capacity to correct the metabolic disturbances associated with diabetes. Moreover, the decreased in body weight of rats after induction of diabetes, and increased in body weight of rats after treatment with MELC was observed. Further, the extract decreased total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL), very LDL (VLDL) levels, and increased high-density lipoprotein (HDL) levels. At the same time MELC treated diabetic rats, reduction in serum aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatise (ALP) activities may be due to the presence of flavonoids and tannins in the plant extract, which repairs the tissue damage induced by diabetic complications. The present investigation suggested that the administration of MELC exhibited antidiabetic activity in STZ-induced diabetic rats and could be considered for further evaluation in drug development.

Keywords: *Lantana camara* Linn, Antihyperglycemic, Antihyperlipidemic activity, Glibenclamide, Streptozotocin.

INTRODUCTION

Diabetes mellitus is a group of metabolic disorders characterized by a high blood glucose level that results from defects in insulin secretion. In general, blood glucose levels are tightly controlled by insulin, a hormone produced by the pancreas [1]. World Health Organization (WHO) suggests that worldwide the global population is in the midst of diabetes epidemic with people in Southeast Asia and Western Pacific being mostly at risk. The number of cases for diabetes that currently at 171 million is predicted to reach 366 million by year 2030 [2]. Diabetes mellitus is classified in two types, insulin dependent diabetes mellitus (IDDM, type 1) and non insulin dependent diabetes mellitus (NIDM, type 2). Type 1 diabetes is an autoimmune disease characterized by local inflammatory reaction in and round islets that is followed by selective destruction of insulin secreting β-cells. Type 2 diabetes is characterized by peripheral insulin resistenace and impaired insulin secretion [3]. Increased production of superoxides and lowered antioxidant enzyme activities compromising with body antioxidant defense systems in hyperglycemia is associated with the pathogenesis of diabetic dyslipidemia, micro- and macrovascular complications. Currently available for the treatment of diabetes mellitus include oral

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hypoglycemic agents and insulin. However these current drugs are not free from side effects [4].

The plant *Lantana camara* L family *Verbenaceae* is available throughout central and south India in most dry stony hills and black soil. chemical constitution for lantana camara is caryophyllene, 1-α-phellandrene, lantadene A, lantadene B, lancamarone quinine, lantanine. Analysis of the volatile oil of leaf of Lantana camara Linn showed that major components such as a pinene, camphene, ß –pinene, myrcene, 1-8 cineole [5]. Previously various activity have reported on Lanata camara Linn some of these are antimycobacterial activity [6], antibacterial [7], cytotoxic [8], wound healing [9], hepatotoxic [10], nematicidal activity [11], insecticidal activity [12], antimotility activity [13], invitro cytotoxic activity [14]. Lanata camara Linn having promising chemical constituents to show various biological activities. The objective of the present work to evaluate the antidiabetic, antihyperlipidaemic activity of *Lantana camara* Linn leaves by using animal models.

MATERIALS AND METHODS

Plant Material

The plant *Lantana camara* Linn, were collected from Komarapalayam, Tamilnadu, India. Care was taken regarding the age and the health of the plant to obtain a best condition leaves. *Lantana camara* Linn leaves were washed properly and dried in shade at room temperature. Leaves were made into fine powder using a mechanical grinder.

Preparation of plant extract

The powder was extracted with hexane to remove lipids. It was then filtered and the filtrate was discarded. The residue was successively extracted with methanol using Soxhlet apparatus [15]. The extract was dried under reduced pressure and stored in a desiccator. The yield of extract was 9.97% w/w.

Preliminary phytochemical screening

One gram of the methanol extracts of *Lantana camara* Linn leaves was dissolved in 100 ml of its own mother solvents to obtain a stock of concentration 1% (v/v). The extracts thus obtained were subjected to preliminary phytochemical screening [15-18].

Animals

Wistar albino rats of either sex weighing between 150- 250 g were used. They were maintained under standard laboratory conditions at a temperature of 23±2°C, with 12 h light - dark cycle, and relative humidity (50 10%). The animals were fed with standard food pellets (Hindustan Lever Ltd, India) and water ad libitum. All animal procedures have been approved and prior permission from the Institutional Animal Ethical Committee was obtained as per the prescribed guidelines.

Acute toxicity studies

Acute oral toxicity study was performed as per OECD-423 guidelines (acute toxic class method). Wistar rats (n = 6) of either sex selected by random sampling technique were used for the study. The animals were kept fasting for overnight providing only water, after which the extract (methanol) were administered orally at the dose level of 5 mg/kg body weight by intragastric tube and observed for 14 days. If mortality was observed in 2 -3 animals, then the dose administered was assigned as toxic dose. If mortality was observed in one animal, then the same dose was repeated again to confirm the toxic dose. If mortality was not observed, the procedure was repeated for further higher dose such as 50, 300 and 2000 mg/kg body weight [19].

Oral glucose tolerance test (OGTT)

The oral glucose tolerance test was performed in overnight fasted (18 h) normal rats. They were divided into four groups (n = 6). Group I served as normal control which received 1% w/v Tween 80 solution and Group II and Group III received methanol extract of *Lantana camara* L (MELC) leaves orally at the doses of 200 and 400 mg/kg respectively, whereas Group IV received glibenclamide (5mg/kg). The blood glucose levels were determined in the following pattern: 0 min. and 30 min to assess the effect of test samples on normal blood glucose rats. The rats were then administered orally with 2g/kg glucose and the glucose levels were determined at 60, 90, 120 and 180 min after glucose load. Blood was collected from the tip of the tail vein and fasting blood glucose level was measured using single touch glucometer [20].

Induction of Diabetes Mellitus

Thirty four rats were subjected to streptozotocin induced diabetes was made by our standard method as mention earlier [21]. In brief, twenty four hour fasting rats were subjected to a single intramuscular injection of streptozotocin (STZ) at the dose of 4mg/ 0.1ml of citrate buffer (pH 4.5)/100gm body weight/rat that produce diabetes after 24 h of injection. Diabetic state was monitored for its stability for next seven days out of thirty four rats, thirty rats with stable diabetes having fasting blood glucose level more than 250 mg/dl were selected as diabetic in this experiment.

Experimental design

Diabetes was induced in rats within 48 hours by the intra peritoneal administration of streptozotocin dissolved in distilled water (5%) in a dose of 100mg/kg body weight. The rats were divided into 5 groups of 6 animals each.

Group I served as normal control received saline,
Group II served as diabetic control received saline,
Group III and IV received 200 and 400 mg/kg methanol extract of *Lantana camara* L (MELC) leaves respectively,

Group V received glibenclamide (5 mg/kg) and served as standard.

Standard drug and extract were prepared in 0.5% carboxy methyl cellulose suspension as vehicle and administered orally, treatment for Group III – V was continued for 21 consecutive days, blood was collected on 0^{th} (before treatment), 7^{th} , 14^{th}, 21^{st} day to investigate different biochemical parameters [22-24].

Estimation of mean body weight and biochemical parameters

Mean body weight was measured during treatment on weekly basis. Blood samples were collected from tip of rat tail and blood glucose levels were estimated using one touch glucometer (Glucocheck, New Delhi) on 0^{th}, 7^{th}, 14^{th} and 21^{st} day. Serum was also analyzed after 21 days treatment for plasma insulin, Glycosylated hemoglobin (HbA_1C), total cholesterol (TC), triglycerides (TG), high density lipoprotein (HDL), low density lipoprotein (LDL), very low density lipoprotein (VLDL), aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatise (ALP) by using standard commercial diagnostic kits (Agappe Diagnostics, Kerala) following the manufacturer's instruction in a semi auto analyzer (Mispa Excel Chemistry Analyser, Mumbai) [25-27].

Histopathology

The dissected liver and pancreas was collected in 10% formalin solution, and immediately processed by the paraffin technique. Sections of 5µ thickness were cut and stained by haematoxylin and eosin for histological examination [28].

Statistical analysis

Values were expressed as mean ± standard error mean (S.E.M) and analyzed using statistical package for social science (SPSS) version 10.0 using ANOVA followed by Dunnett's test, $P< 0.05$ were considered statistically significant.

RESULTS

Preliminary phytochemical screening

Preliminary phytochemical screening of the MELC shows the presence of carbohydrates, flavonoids, phytosterols, saponins, tannins, phenolic compounds and fixed oils.

Acute toxicity study

Limit test at 2000 mg/kg body weight was selected to perform acute toxicity of MELC laboratory animals. In LD_{50} studies, it was found that the animals were safe up to a maximum dose of 2000 mg/kg body weight. There were no changes in normal behaviour pattern and no signs and symptoms of toxicity and mortality were observed.

Selection of dose

The LD_{50} of MELC as per OECD guidelines falls under class four values with no signs of acute toxicity at 2000 mg/kg. The pharmacological evaluations were carried out at doses of 200 to 400 mg/kg body weights.

Effect on oral glucose tolerance test

The effects of MELC on the plasma glucose level are shown in table 1. After administration of glucose in rats the rise in glucose level was observed in glucose control, extract treated and standard group. In rats treated with MELC, there was a significant reduction in plasma glucose level, while in glucose control rats the plasma glucose level increased. Meanwhile same results were observed in glibenclamide treated group.

Effect on blood glucose level

There was a significant increase in blood glucose level in diabetic rats when compared with normal controls due to injection of STZ. In the study, daily administration of the MELC for three weeks led to a dose dependent fall in blood glucose levels. At the end of experiment (the 21st day) blood glucose level was (264.18 ± 18.26) and (172.43± 15.64) mg/dL at the doses of 200 and 400 mg/kg of MELC respectively. The antidiabetic effect of MELC on the blood glucose levels in diabetic rats is also shown in table 2.

Effect of plasma insulin and HbA_1C level

In STZ - induced diabetic rats showed a significantly ($p<0.01$) increase in the level of HbA_1C and reduction of plasma insulin level when compared with normal control rats. In diabetic rats, administration of MELC 200 and 400 mg/kg dose showed significant ($P<0.001$) reduction in HbA_1C level compared to diabetic control rats. Also, a significantly ($P<0.05$) increased level of plasma insulin was observed in diabetic rats treated with both doses of MELC and glibenclamide compared to diabetic control rats (Table 4).

Effect on body weight

The body weight of the diabetic controls (group II) significantly decreased compared with the normal controls (group I). During the weekly of observation of the MELC treated diabetic rats at doses of 200 mg/kg and 400 mg/ kg, there were significant ($P <0.05$) weight gains on day 21 relative to day 0 as shown in table 4.

Effect on lipid profile

In STZ-induced diabetic rats, TC, TG, LDL, and VLDL levels were increased and HDL level was decreased significantly ($P<0.001$) compared to normal control rats. In diabetic rats, administration of MELC 200 and 400 mg/kg dose showed significant ($P<0.001$) reduction in elevated TC, TG, LDL and VLDL levels compared to diabetic control rats. Also, a significantly ($P<0.05$) increased level of HDL was observed in diabetic rats treated with both

doses of MELC and glibenclamide compared to diabetic control rats (Table 5 & 6).

Effect on liver markers

In STZ-induced diabetic rats, AST, ALT and ALP levels were increased significantly (P<0.001) compared to normal control rats. In diabetic rats, administration of MELC 200 and 400 mg/kg dose showed significant (P<0.001) reduction in elevated AST, ALT and ALP levels compared to diabetic control rats. The glibenclamide treated rats also showed a significant ($P < 0.01$) decrease in the activities of the above-mentioned enzymes (Table 7).

Histopathological studies

Histology of liver in experimental rats was determined after 21days of treatment. Normal control — normal liver showing normal hepatic cells and architecture, Hepatocytes with prominent nuclei, sinusoids, portal Vienne, and hepatic artery. Diabetic control — Showed loss of normal architecture, cellular necrosis and foci of hemorrhage liver structure in STZ induced rat. Diabetic + MELC (200 mg/kg, 400 mg/kg) — section of liver showing normal architecture of liver cells, Hepatic sinusoids appear in normal. The nuclei are round & uniform with little variation in size. Diabetic + glibenclamide (5 mg/kg) — section of liver showing normal hepatocellular architecture with normal nucleus, Hepatic sinusoids appear in normal (Figure 1). Histology of pancreas in experimental rats was evaluated after 21 days of treatment. Normal control — presence of normal pancreatic islet cells. Diabetic control — degranulated and dilated islet cells. Diabetic + MELC (200mg/kg, 400mg/kg) — granulated pancreatic islets, showing prominent hyper plasticity islet. Diabetic + glibenclamide (5 mg/kg) Islets are compactly arranged, narrowed acinar and islet cells (Figure 2).

Discussion

STZ produces oxygen radicals in the body, which cause pancreatic injury and could be responsible for increased blood glucose in animals (29). STZ- induced diabetes may be due to vitiate glucose oxidation and reduction of insulin biosynthesis and secretion. The toxicity of STZ is due to DNA alkylation of its methyl nitrosourea moiety mainly at O^6 position of guanine (30). The transfer of methyl group from STZ to the DNA molecule causes damage which results in fragmentation of DNA and functional defects of the beta cells. Moreover, STZ is potential to act as an intracellular nitric acid (NO) donor and generates reactive oxygen species (ROS). The synergistic action of both NO and ROS may also contribute to DNA fragmentation and other deleterious changes caused by STZ (31). In our study, elevated blood glucose level and decreased insulin level were observed in STZ-induced diabetic rats and it may be due to above stated mechanism of STZ. Oral administration of MELC 200, 400 mg/kg and glibenclamide 5 mg/kg to the diabetic rats significantly reduced blood glucose level from the first week to the third week compared to diabetic rats. Also the decreased insulin levels were noticed in diabetic rats compared to normal control rats which directly support and represent STZ-mediated beta cell destruction or damage. In diabetic rats, treatment with MELC and Glibenclamide increased the insulin level compared to diabetic control rats. Hence, the hypoglycaemic activity of MELC may be due to its pancreatic action against STZ-mediated damage to the pancreatic beta cell and also possibly because of regeneration of damaged beta cells or increased insulin release or action.

Loss of body weight is due to increased muscle destruction and loss of proteins contents in the tissue (32). Diabetic rats treated with the MELC showed an improvement in body weight in comparison to the diabetic control and standard glibenclamide treated groups, which signifies its protective effect in controlling muscle wasting i.e. reversal of gluconeogenesis. Moreover, the ability to protect body weight loss seems to be as a result of its ability to reduce hyperglycemia.

HbA1c is the product of non-enzymatic reaction between glucose and free amino groups of Hb (glycosylation) (33). It is a marker of evaluation of long-term glycemic control in diabetic patients and predicts risks for the development and/or progression of diabetic complications (34). Our study results showed that increased level of HbA1c was oserved in diabetic rats compared to normal control rats which indicates the occurrence of glycosylation in diabetic rats due to hyperglycemia. Administration of MELC and glibenclamide to the diabetic rats significantly reduced HbA1c levels compared to diabetic control rats. This action represents that MELC has an ability to prevent the development of diabetes-associated complications. Increase in concentration of TC, TG, LDL, VLDL and decreased HDL is observed in diabetic control rats, Hyperlipidemia is a recognized consequence of diabetes mellitus and a risk factor for coronary heart disease. Under normal circumstances, insulin activates the enzyme lipoprotein lipase, which hydrolyses triglycerides. However in diabetic state, lipoprotein lipase is not activated due to insulin deficiency, resulting in hypertriglyceridemia and hypercholesterolemia caused by derangement of metabolic abnormalities (35). The elevated levels of LDL in diabetic control rats might be due to the stimulation of hepatic triglyceride synthesis as a result of free fatty acid influx (36). Administration of MELC and glibenclamide normalized serum lipids, secondary to the diabetic state. Diabetes induced hyperlipidemia is attributable of excess mobilization of fat from the adipose tissue due to the under utilization of glucose.

The activity of AST, ALT, and ALP was found to be significantly increased in diabetic rats when compared to the normal rats. This may be due to the cellular damage to liver caused by STZ which leads to leakage of enzymes from cytosol into the bloodstream (37). Administration of

MELC and glibenclamide to the diabetic rats significantly reduced the AST, ALT and ALP levels were compared to diabetic control rats. The hepatoprotective agent flavonoid present in plant extract might have involved in the reduced activities of AST (38) thereby inactivating cytosolic AST within the diabetic rat tissues through a glycation reaction (39). In the MELC treated diabetic rats, reduction in ALT and ALP activities may be due to the presence of flavonoids and tannins in the plant extract, which repairs the tissue damage induced by diabetic complications (40). Histopathological studies of pancreas and liver in diabetic and extract treated groups substantiate the cytoprotective action of extract.

Table 1: Effect of MELC and Glibenclamide on oral glucose tolerance of normoglycemic rats (OGTT)

Group	Treatment	Blood glucose level (mg/dL)					
		0 mins	30 mins	60 mins	90 mins	120 mins	180 mins
I	Normal Control	88.34± 2.27	132.43±3.70	125.40± 4.16	111.33± 4.94	99.57± 2.84	82.96± 3.42
II	MELC 200 mg/kg	65.87± 1.26	129.87±4.62[b]	141.57± 3.37[c]	132.85± 3.30[a]	120.36± 5.10[a]	112.47± 3.29[a]
III	MELC 400 mg/kg	69.05± 2.47	105.73± 5.31[a]	119.94±2.52[a]	106.77± 3.13[a]	94.36± 3.67[a]	75.69± 5.10[a]
IV	Glibenclamide 5 mg/kg	70.97± 2.53	100.57± 2.13[a]	122.64± 3.21[a]	109.61± 3.95[a]	90.47± 3.79[a]	72.87± 4.68[a]

Values are given as mean ± S.E.M for groups of six animals each. Values are statistically significant at *p<0.05. ([a] = p<0.001; [b] = p<0.01; [c] = p<0.05) MELC treated groups (II, III) and standard group (IV) were compared with control (I) group.

Table 2: Effect of MELC and Glibenclamide on blood glucose level of control and experimental groups of rats

Group	Treatment	Blood glucose level (mg/dL)			
		Day 0	Day 7	Day 14	Day 21
I.	Normal Control rats	85.58± 3.16	89.23± 3.12	90.01± 3.80	85.13± 3.08
II.	Diabetic Control rats	368.18± 8.19	372.11± 13.43	389.1± 12.09	395.10± 14.14
III.	Diabetic group + MELC (200 mg/kg)	363.14± 9.42[a]	349.74± 6.48[a]	299.14±6.90[a]	264.18 ± 18.26[b]
IV.	Diabetic group + MELC (400 mg/kg)	336.19± 12.83[a]	257.87± 14.72[a]	223.10± 10.81[a]	172.43± 15.64[a]
V.	Diabetic group +Glibenclamide (5mg/kg)	297.25± 12.09	238.90± 12.47	194.95± 16.88[b]	169.93± 14.91[c]

Values are given as mean ± S.E.M for groups of six animals each. Values are statistically significant at *p<0.05. ([a] = p<0.001; [b] = p<0.01; [c] = p<0.05). MELC treated diabetic groups (III, IV) were compared with diabetic control group (II) and standard group (V).

Table 3: Effect of MELC and Glibenclamide on plasma insulin, $HbA1_C$ of control and experimental groups of rats

Groups	Treatment	Insulin µU/ml	$HbA1_{c\ \%}$
I	Normal Control rats	32.11 ± 1.84	3.90 ± 0.74
II	Diabetic Control rats	16.57 ± 1.50[b]	7.11 ± 0.63[b]
III	Diabetic group + MELC (200 mg/kg)	22.43 ±1.93[c]	5.98 ±0.70[a]
IV	Diabetic group + MELC (400 mg/kg)	32.45 ± 1.98[a]	4.12 ± 0.27[a]
V	Diabetic group + Glibenclamide (5mg/kg)	33.06 ± 2.45[b]	3.78 ± 0.19[c]

Values are given as mean ± S.E.M for groups of six animals each. Values are statistically significant at *p<0.05. ([a] = p<0.001; [b] = p<0.01; [c] = p<0.05). MELC treated diabetic groups (III, IV) were compared with diabetic control (II) group and standard group (V).

Table 4: Effect of Body weight changes in MELC and Glibenclamide on control and experimental groups of rats

Group	Treatment/Dose	Body weight (g) Initial	Body weight (g) Final
I.	Normal Control rats	198.19 ± 9.27	209.18± 11.43
II.	Diabetic Control rats	209.48±10.14	168.96±9.71
III.	Diabetic group + MELC(200mg/kg)	214.35± 5.19[a]	235.16± 8.04[b]
IV.	Diabetic rats + MELC(400 mg/kg)	194.08± 12.93[a]	221.90± 12.70[c]
V.	Diabetic rats+ Glibenclamide (5mg/kg)	207.41± 14.08[b]	239.15± 16.52[a]

Values are given as mean ± S.E.M for groups of six animals each. Values are statistically significant at *p<0.05. ([a] = p<0.001; [b] = p<0.01; [c] = p<0.05) MELC treated diabetic groups (III, IV) were compared with diabetic control group (II) and standard group (V).

Table 5: Effects of MELC and Glibenclamide on Total cholesterol, Triglycerides levels of control and experimental groups of rats.

Group	Treatment/Dose	Total Cholesterol (mg/dl)	Triglycerides(mg/dl)
I	Normal Control group	155.72 ± 2.41	79.57 ± 2.95
II	Diabetic control rats	258.15 ± 5.70	189.27 ±5.87
III	Diabetic rats + MELC (200 mg/kg)	221.45±3.09[b]	156.72±3.74[a]
IV	Diabetic rats + MELC (400 mg/kg)	159.75±4.34[c]	85.46± 6.45[a]
V	Diabetic rats +Glibenclamide (5 mg /kg)	150.38.± 5.94[c]	80.63 ± 6.25[a]

Values are given as mean ± S.E.M for groups of six animals each. Values are statistically significant at *p<0.05. ([a] = p<0.001; [b] = p<0.01; [c] = p<0.05). MELC treated diabetic groups (III, IV) were compared with diabetic control group (II) and standard group (V).

Table 6: Effect of MELC and Glibenclamide on HDL, LDL, VLDL of control and experimental groups of rats

Group	Treatment/Dose	HDL cholesterol (mg/dl)	LDL cholesterol (mg/dl)	VLDL cholesterol (mg/dl)
I	Normal Control rats	35.30 ± 2.11	95.47 ± 1.50	15.74± 2.58
II	Diabetic control rats	30.63 ± 1.98	197.11 ± 2.63	34.78 ± 2.47
III	Diabetic rats + MELC (200 mg/kg)	32.11±1.74[a]	135.89±3.75[c]	23.96±1.73[b]
IV	Diabetic rats + MELC (400 mg/kg)	34.98 ± 0.47[c]	92.75 ± 4.26[a]	18.98 ± 1.98[a]
V	Diabetic rats+ GlGlibenclamide (5mg/kg)	38.97 ± 3.04[b]	95.10 ± 3.24[b]	16.78 ± 2.57[c]

Values are given as mean ± S.E.M for groups of six animals each. Values are statistically significant at *p<0.05. ([a] = p<0.001; [b] = p<0.01; [c] = p<0.05). MELC treated diabetic groups (III, IV) were compared with diabetic control group (II) and standard group (V).

Table 7: Effect of MELC and Glibenclamide on AST, ALT, ALP of control and experimental groups of rats

Group	Treatment/Dose	AST (U/L)	ALT (U/L)	ALP (U/L)
I	Normal Control rats	115.85± 12.11	45.89± 5.47	255.74± 8.58
II	Diabetic control rats	266.63± 14.98	78.11± 8.43	374.78± 18.87
III	Diabetic rats + MELC (200 mg/kg)	142.71±13.74[a]	55.89±9.85[c]	290.96±14.73[b]
IV	Diabetic rats + MELC (400 mg/kg)	120.98 ± 12.87[c]	47.59± 10.26[a]	261.98± 15.98[a]
V	Diabetic rats+ GlGlibenclamide 5mg/kg)	38.97± 3.04[b]	95.10± 3.24[b]	16.78± 2.57[c]

Values are given as mean ± S.E.M for groups of six animals each. Values are statistically significant at *p<0.05. ([a] = p<0.001; [b] = p<0.01; [c] = p<0.05). MELC treated diabetic groups (III, IV) were compared with diabetic control group (II) and standard group (V).

Figure 1: Histology of liver in experimental rats after 21 days of treatment. A - Normal control showed normal liver showing normal hepatic cells and architecture.B - Diabetic control Showed loss of normal architecture, cellular necrosis and foci of hemorrhage liver structure. C & D - Diabetic + MELC (200 mg/kg, 400 mg/kg) showed normal architecture of liver cells, Hepatic sinusoids appear in normal. E - Diabetic + glibenclamide (5 mg/kg) showed normal hepatocellular architecture with normal nucleus.

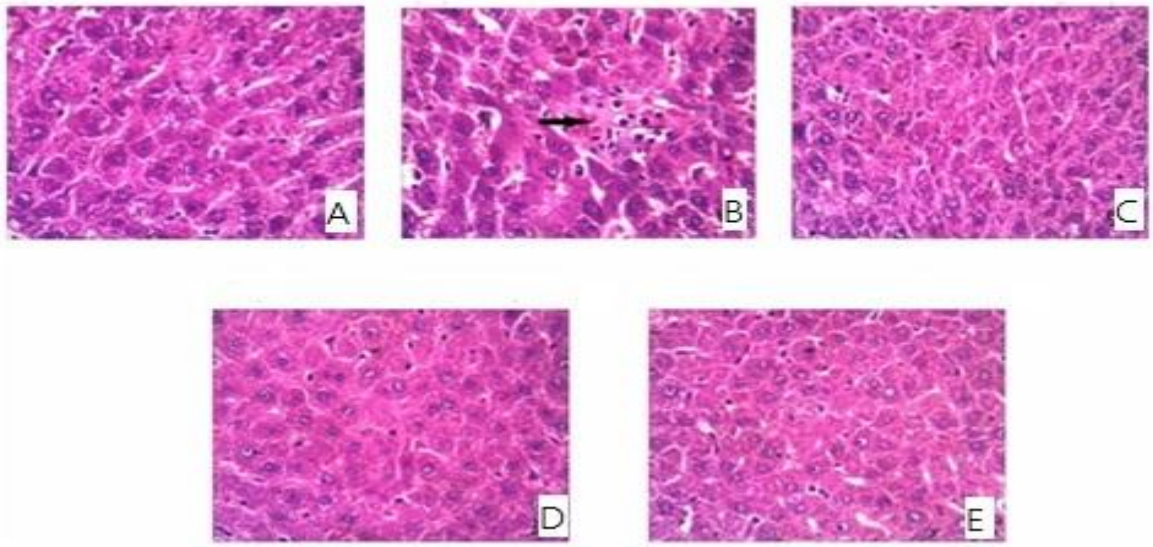
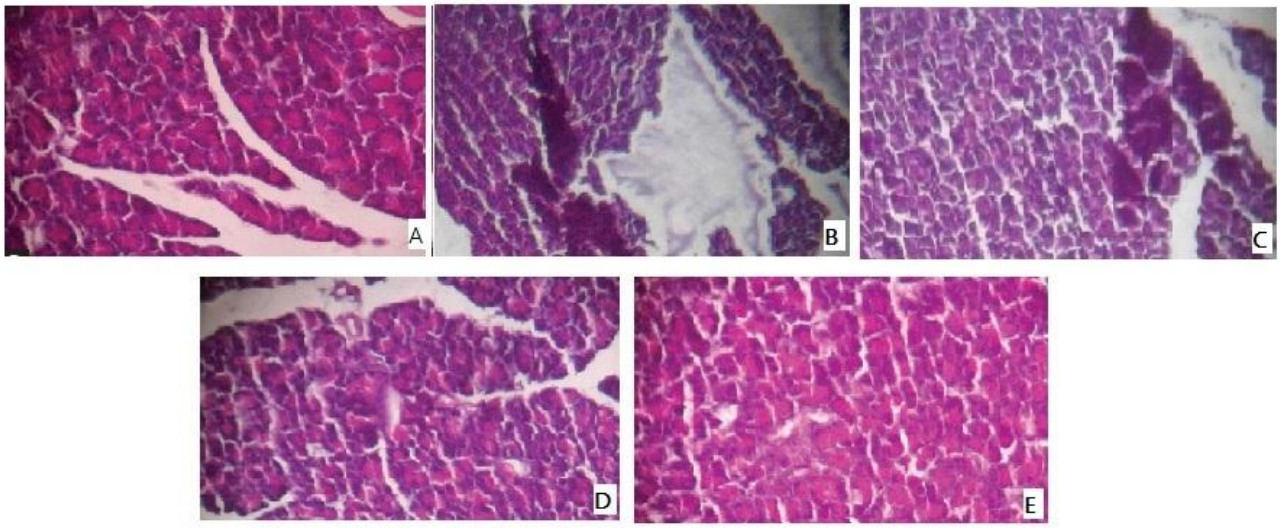


Figure 2: Histology of pancreas in experimental rats after 21 days of treatment. A - Normal control — presence of normal pancreatic islet cells. B - Diabetic control — degranulated and dilated islet cells. C&D - Diabetic + MELC (200mg/kg, 400mg/kg) — granulated pancreatic islets, showing prominent hyper plasticity islet. E - Diabetic + glibenclamide (5 mg/kg) Islets are compactly arranged, narrowed acinar and islet cells.



CONCLUSION

In present study, we selected *Lantana camara* Linn leaves to evaluate its antidiabetic activity owing to its traditional uses. The findings of study exhibited that the oral administration of methanol extract of leaves of *Lantana camara* Linn exhibited significant antidiabetic effect in controlling the blood glucose level. Additionally, the extract decreased total cholesterol, triglycerides, LDL, VLDL, AST, ALT and ALP with increase in HDL at the end of the treatment. This confirms the potent antidiabetic effect of extract. The methanol extract of leaves exhibited maximum antidiabetic activity as compared to standard Glibenclamide. The findings of the present study suggest that the methanolic leaves extract of *Lantana camara* Linn possesses significant antihy perglycemic and antihy perlipidemic activities in STZ-induced diabetic rats. Further, the extract might be beneficial for future drug design and development so as to be effective for the management of diabetes mellitus.

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