Research Article

Evaluation of Antidiabetic Potential of *Caesalpinia pulcherrima* (L.) Swartz Leaf Extract in Alloxan Induced Diabetic Rats

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ABSTRACT

Objectives: The present study was designed to evaluate the antidiabetic activity of *Caesalpinia pulcherrima (L.) Sw.* leaf extract in alloxan-induced diabetic rats.

Materials and Methods: The leaves of *Caesalpinia pulcherrima (L.) Sw.* (CP) were collected and extracted to yield methanolic extract. CP extract was subjected for preliminary phytochemical analysis, estimation of total flavonoid content and total phenolic content. Type 1 diabetes was induced by intraperitoneal injection of Alloxan (80 mg/kg) in male Wistar rats. Rats were divided into groups and treated with CP extract (100 mg/kg &200 mg/kg) for 21 days. Oral glucose tolerance test was conducted in both normal and diabetic rats. Blood glucose levels were monitored throughout the study. At the end, serum lipid profiles were assessed, and pancreatic tissues were collected for histopathological analysis.

Results: The *Caesalpinia pulcherrima (L.) Sw.* leaves were powdered and extracted using methanol via Soxhlet method. Phytochemical screening revealed the presence of carbohydrates, flavonoids, saponins, tannins, alkaloids, terpenoids, amino acids, and phenols. Administration of CP extract (100 & 200 mg/kg) showed significant ($p < 0.01$ & $p < 0.001$ respectively) reduction in the above levels and improved glucose tolerance suggesting that there was an improvement in alloxan induced diabetes. In addition, CP treatment increased size of islets which showed regenerative effects on ß-cells in histopathology study.

Conclusion: These results suggest that CP improved Alloxan-induced hyperglycemia and abnormal lipid level and these effects may be mediated by interacting with multiple targets operating in diabetes mellitus.

Keywords: Diabetes mellitus, Caesalpinia pulcherrima (L.) Sw., Alloxan, β-cells.

INTRODUCTION

Diabetes mellitus (DM) is defined as a state of hyperglycemia in either fasting or post-meal state[1]. In Greek, diabetes means "to pass through" and mellitus is the Latin word for honey (referring to sweetness) [2]. A deficiency or ineffective production of insulin by the pancreatic β-cells in the islets of Langerhans leads to fluctuations in blood glucose levels, either increasing or decreasing its concentration. It is found to damage many of body systems particularly blood vessels, eyes, kidney, heart and nerves. DM has been classified into three types i.e. insulin dependent diabetes mellitus (IDDM, Type I), non-insulin dependent diabetes mellitus (NIDDM, Type II) and Gestational diabetes mellitus[3].

Diabetes mellitus (DM) is a rapidly growing global metabolic disorder, with cases rising from 108 million in 1980 to 422 million in 2014. The prevalence among adults increased from 4.7% to 8.5% during the same period. WHO projects DM to become the 7th leading cause of death by 2030. Type 1 DM (T1DM), typically seen in childhood, accounts for 5–10% of cases, while Type 2 DM (T2DM) comprises 90–95%. Gestational diabetes mellitus (GDM), affecting 5–15% of pregnancies, may lead to DM in 40–60% of women within 5–10 years. Uncontrolled DM can trigger complications such as cardiovascular disease, renal failure, blindness, hypertension, and neuropathy[4].

The treatment of hyperglycemia varies depending on the type of DM. Type 1 DM requires immediate insulin therapy. In Type 2 DM, management involves lifestyle changes and typically begins with glibenclamide. Further treatment decisions depend on contraindications, drug interactions, cost, side effects, and efficacy[5]. Insulin therapy, once considered a last resort for Type 2 diabetes, is now prescribed earlier due to its proven benefits. However, it carries a risk of hypoglycaemia (low blood sugar) [6].

Conventional oral hypoglycemic drugs often cause side effects and are costly. In contrast, herbal medicines offer a safer, more affordable alternative with minimal adverse effects. Many antidiabetic plants stimulate insulin release from pancreatic islets and enhance insulin sensitivity. Hence, identifying and isolating plant-derived antihyperglycemic compounds has gained increasing importance[7].

Caesalpinia pulcherrima L. Swartz (Leguminosae) is an ornamental plant due to its variety of flowers, which appear yellow, pink, off white and red with yellow margins. Phytochemical investigations on *Caesalpinia pulcherrima* have revealed the presence of various phyto active constituents such as glycosides, rotenoids, isoflavones, flavanones, chalcones, flavanols, flavones and sterols[8].

C. pulcherrima also known as 'Pride of Barbados' locally known as "Radhachura," belongs to the Fabaceae family,

distributed mainly in West Bengal, Tamilnadu, Kerala, Karnataka and throughout India. This plant has some impressive health benefits, found to possess antitumor, antimicrobial, abortifacient, cardioprotective, lipid-lowering, hepato-protective, antiulcer, antiasthma, and hypoglycemic activities[9].

To best of our knowledge evaluation of anti-diabetic activity of leaf extract of *Caesalpinia pulcherrima* in rats has not been carried out, hence this work is proposed to be undertaken.

MATERIALS AND METHODS

Plant materials and chemicals

The leaves of *Caesalpinia pulcherrima* were collected from surrounding areas of Dharwad, Karnataka, and authentication of the plant was done taxonomist, Dr. M. Jayaraj, Professor, Department of Botany, Karnataka University Dharwad. The collected material was washed with running water. The leaves were dried under shade. Dried leaves were coarsely powdered and used for extraction.

Analytical-grade chemicals and reagents were utilized throughout the study. Alloxan was sourced from Sigma-Aldrich, while glibenclamide was provided by Aventis Pharma. Methanol, pet-ether, diethyl ether, and formalin were procured from S.D. Fine Chemicals. For biochemical analysis, triglyceride, total cholesterol, HDL-c, serum glucose level, urea and creatinine estimation kit was obtained from the obtained from Swemed Diagnostics, Bangalore.

Experimental Animals:

Male albino Wistar rats weighing between 180–200 g were selected for the study. The animals were obtained from the National Institute of Bioscience, Pune, Maharashtra, and housed in the animal facility at SET's College of Pharmacy, Dharwad. They were kept under controlled environmental conditions, including a temperature range of 20–25 °C, relative humidity of 50 ± 5%, and a 12-hour light/dark cycle. Each rat was housed individually in clean polypropylene cages with sterile paddy husk bedding. Standard pellet feed and water were provided ad libitum. Prior to the experiment, the animals underwent a seven-day acclimatization period, followed by 48 hours of habituation to reduce non-specific stress.

All experimental procedures were reviewed and approved by the Institutional Animal Ethical Committee (IAEC), SET's College of Pharmacy, Dharwad, under proposal number SETCPD/IAEC/JUNE/2025/003, in accordance with CPCSEA guidelines (Reg. No. 112/PO/Re/S/99/CPCSEA), Government of India.

Preparation of the extract:

Authenticated leaves of *Caesalpinia pulcherrima* were shade dried and pulverized in to coarse material. Coarse plant material was cleaned by passing the powder material through 120 mesh sieves to remove any fine dust or powder, and coarse powder was used for extraction. Dried leaf exhaustively extracted using methanol in a Soxhlet apparatus. The extract was concentrated by rotary flash evaporator, under reduced pressure and controlled temperature, followed by drying and stored in a desiccator.

Phytochemical investigation:

Preliminary phytochemical screening of the plant extract was performed for determining the presence of Alkaloids, Saponin, Carbohydrates, Flavonoids, Terpinoids, Tannins, Amino acids and Phenolic compounds[10].

Pharmacological evaluation

Alloxan induction in rats

The acclimatized rats were kept fasting for 24 hrs with water ad libitum. Alloxan which was freshly prepared in normal saline was administered at a single dose of 80 mg/kg body wt. to the overnight fasted rats. Animals were observed to develop diabetes for 5 days[11].

Experimental Design

Rats were considered diabetic when the blood glucose level has been raised beyond 200 mg/100 ml of blood. This condition was observed at the end of 48 hrs after Alloxanisation. The 30 rats will be segregated into five groups of six rats in each.

- **Group I:** Normal Control (Distilled Water)
- **Group II:** Diabetic control (Alloxan 80 mg/kg i.p. prepared in normal saline)[11]
- **Group III:** Test-1 (*Caesalpinia pulcherrima* (L) leaves extract 100 mg/kg/day p.o.+ Alloxan 80 mg/kg i.p.)
- **Group IV:** Test-2 (*Caesalpinia pulcherrima* (L) leaves extract 200 mg/kg/day p.o + Alloxan 80 mg/kg i.p.)
- **Group V:** Standard (Glibenclamide 2.5 mg/kg p.o) + Alloxan 80 mg/kg i.p. [12].

Group I, received only normal saline throughout the course of experiment was used as control. Group II, receives intraperitoneal injection of alloxan (80mg/kg). Group III and IV received alloxan(80mg/kg) i.p and test drug at doses of 100mg/kg and 200mg/kg b.w. respectively. Group V received alloxan(80mg/kg) i.p and glibenclamide (2.5mg/kg). All above treatments were given for 21 days. After 24 hrs of last treatment, rats were anesthetized and Blood was collected by tail vein and allowed to clot for 30 minutes at room temperature. The serum was separated by centrifugation at 2500 rpm at 30°C for 15 minutes and used for the estimation of marker enzymes. After which all the rats were sacrificed, and pancreas were collected for histopathological evaluation.

Determination Of Blood Glucose Levels

Blood samples was collected by cutting the tail-tip of the rats, for blood glucose determination at intervals of 1st, 7th, 14th and 21st day respectively. Determination of the blood

glucose level was done using the one touch glucometer strips and reported as mg/dl[13].

Oral glucose tolerance test (OGTT) in normal and diabetic rats[12]

On 21st day, glucose tolerance of various groups was estimated by a simple OGTT. Glucose (2 gm/kg) was administered to 12 hr fasted rats and Blood samples were collected from tail vein before glucose load (0 min), at 30 min, 60 min and 120 min afterwards. Blood glucose levels were measured using glucometer.

The results are expressed as integrated area under curve for glucose (AUC glucose) calculated by trapezoid rule.

$$\text{AUC glucose} = \frac{(C1+C2)}{2} X\,(t2 - t1)$$

Estimation of biochemical parameters[12]

At the end, blood samples were collected from tail vein. Serum was separated and analyzed spectrophotometrically for triglyceride (STG), total cholesterol (STC), HDL-cholesterol (HDL-c), LDL-cholesterol (LDL- c), serum glucose, urea and creatinine, by using diagnostic reagent kit Swemed Diagnostics, Bangalore.

Histopathological Examination

The whole pancreas from each animal were removed after sacrificing the animal, collected and preserved in 10% formalin solution. The samples were submitted to Jeevan Lab Pvt Ltd. (Belgaum, India) for histological examination[14].

Statistical Analysis

The *in-vivo* data obtained was expressed in mean ± SEM values by using one Way ANOVA test followed by Tukey's test. The values were calculated using graph pad prism version 5.0 Software.

RESULTS

Preliminary qualitative phytochemical analysis

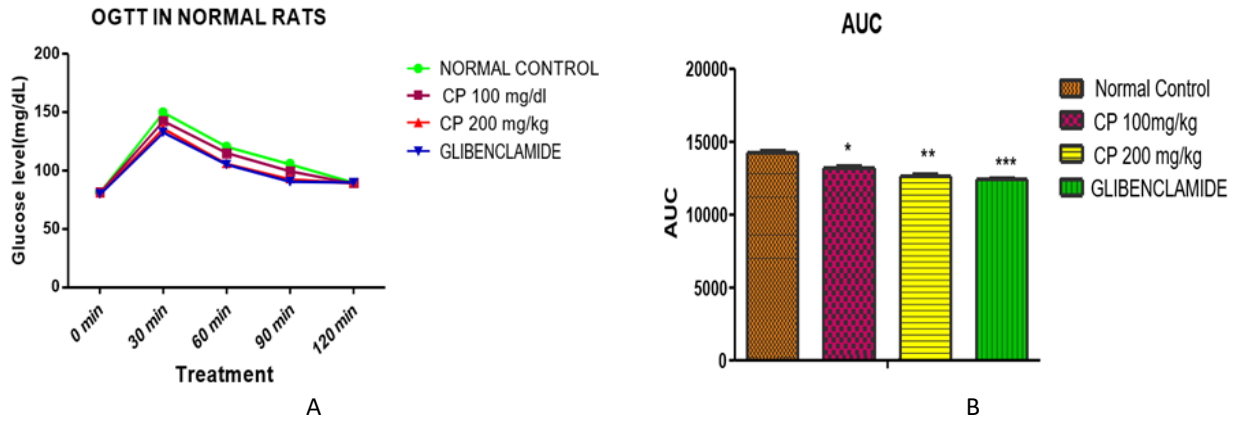
Phytochemical evaluation was carried out on the methanolic leaf extract of *Caesalpinia pulcherrima* using standard qualitative and quantitative techniques. Preliminary screening revealed the presence of Alkaloids, Saponin, Carbohydrates, Flavonoids, Terpinoids, Tannins, Amino acids and Phenolic compounds. Quantitative estimation of total phenolic content (TPC) was performed using the Folin–Ciocalteu method, while total flavonoid content (TFC) was determined spectrophotometrically via the aluminum chloride assay.

Oral Glucose Tolerance Test (OGTT) in Normal Rats

Table 1: Oral glucose tolerance test (OGTT) in normal rats

GROUP	0 min	30 min	60 min	90 min	120 min
CONTROL	81.40±2.205	149.8±1.772	120.4±1.778	111.4±1.631	101.80±1.772
CP 100mg/kg	81.60±2.135	142.2±0.8602	111.0±2.145*	99.60±1.568*	91.00±1.643*
CP 200mg/kg	80.80±2.059	135.8±0.8602**	105.8±1.594***	92.60±0.9274***	89.40±1.208***
GLIBENCLAMIDE (2.5mg/kg)	79.60±1.887	132.6±0.9274**	105.0±1.517***	90.40±0.9274***	88.00±1.789***

Figure 1: Oral glucose tolerance test (OGTT) in normal rats (A, B)



A B

Data represent the mean ± S.E.M., for n=6. * p<0.05, * * p<0.01, ***p<0.001compared to normal control.

The data indicates that both CP 100 mg/kg and CP 200 mg/kg demonstrate significant (p<0.05 and p<0.001 respectively) improvements in glucose tolerance compared to the control group, particularly at the 60, 90, and 120-minute marks. The 200 mg/kg dosage shows the most pronounced effects, significantly (p<0.001) lowering glucose levels at all measured time points. The Glibenclamide treatment also significantly (p<0.001) enhances glucose metabolism, confirming its efficacy as a reference. Overall, these results suggest that CP extract has potential as a therapeutic agent for improving glucose tolerance, particularly beneficial in managing conditions like diabetes.

Table 2: AUC of Normal rats

GROUPS	Mean ± SEM
Control	9259 ± 135
CP 100mg/kg	13860 ± 112.41
CP 200mg/kg	12320 ± 115.26
Glibenclamide (2.5mg/kg)	12287 ± 102.74

The AUC for the CP 100 mg/kg group is 13860 ± 112.41, which is significantly ($p < 0.05$) lower than the control group. The CP 200 mg/kg group shows an AUC of 12320 ± 115.26, which is significantly ($p < 0.001$) lower than both the control. Whereas, Glibenclamide treatment group has an AUC of 12287 ± 102.74, which is also significantly lower than the control group ($p < 0.001$) and similar to the 200 mg/kg CP group.

ORAL GLUCOSE TOLERANCE TEST IN DIABETIC RATS

Table 3: Oral glucose tolerance test (OGTT) in diabetic rats

GROUP	0 min	30 min	60 min	90 min	120 min
DIABETIC CONTROL	287.6±3.415	337.6±1.778	347.8±0.8602	356.4±1.288	351.8±4.420
CP 100mg/kg	280.0±1.789	327.0±1.789*	331.0±4.336**	339.8±4.705**	326.4±5.183**
CP 200mg/kg	279.0±2.881	316.0±3.130**	300.6±1.860***	288.0±2.510***	270.0±1.789***
GLIBENCLAMIDE(2.5mg/kg)	278.4±2.874	306.0±1.817**	296.6±1.364***	279.8±1.772***	270.8±3.153***

The results indicate that both CP 100 mg/kg and CP 200 mg/kg treatments significantly ($p<0.05$ and $p<0.001$ respectively) improve glucose tolerance in diabetic rats compared to the diabetic control group. The 200 mg/kg dose yields the most pronounced effects, leading to significantly lower glucose levels across all time points measured. The Glibenclamide treatment also demonstrates significantly ($p<0.001$) efficacy in regulating glucose levels, confirming its effectiveness as a reference.

Table 4: AUC of diabetic rats

GROUPS	Mean ± SEM
Diabetic Control	14196 ± 133.52
CP 100mg/kg	13173 ± 112.41
CP 200mg/kg	12579 ± 115.26
Glibenclamide (2.5mg/kg)	12354 ± 102.74

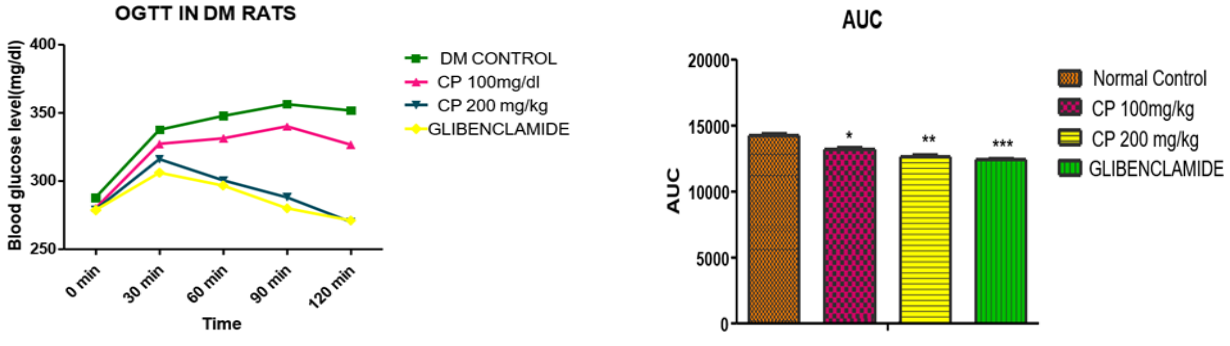
The diabetic control group has the highest AUC at 14196 ± 133.25. This indicates a poor glucose tolerance, as the elevated AUC reflects a significant and prolonged glucose response following the glucose load. This is typical for diabetic conditions, where blood glucose levels remain elevated for longer periods. The AUC for the CP 100 mg/kg group is 13173 ± 112.41, which is significantly lower than the control group ($p < 0.05$). The CP 200 mg/kg group shows an even lower AUC of 12579 ± 115.26 ($p < 0.001$), indicating a pronounced improvement in glucose regulation. This suggests that the higher dosage of CP is more effective in enhancing glucose metabolism and reducing the overall glucose response. However, the Glibenclamide treatment group has an AUC of 12354 ± 102.74 ($p < 0.001$), which is similar to the CP 200 mg/kg group.

EVALUVATION OF CP EXTRACT ON BLOOD GLUCOSE LEVEL IN ALLOXAN-INDUCED DIABETIC RATS

The results (table 5) revealed significant reduction in blood glucose levels over a 21-day period in diabetic rats treated with CP at two different doses (100 mg/kg and 200 mg/kg), as well as with Glibenclamide, compared to the diabetic control group. The diabetic control group showed a progressive increase in glucose levels, rising from 305.0±2.345 mg/dL on the 0th day to 365.6±3.187 mg/dL by the 21st day, indicating worsening hyperglycemia.

In contrast, the CP 100 mg/kg group showed glucose levels with no significant reduction until the 7th day, on 14th day reduction was noted ($p < 0.05$), and further significant decline on the 21st day ($p < 0.01$), suggesting some efficacy in glucose management.

Figure 2: Oral glucose tolerance test (OGTT) in diabetic rats (A, B)



A B

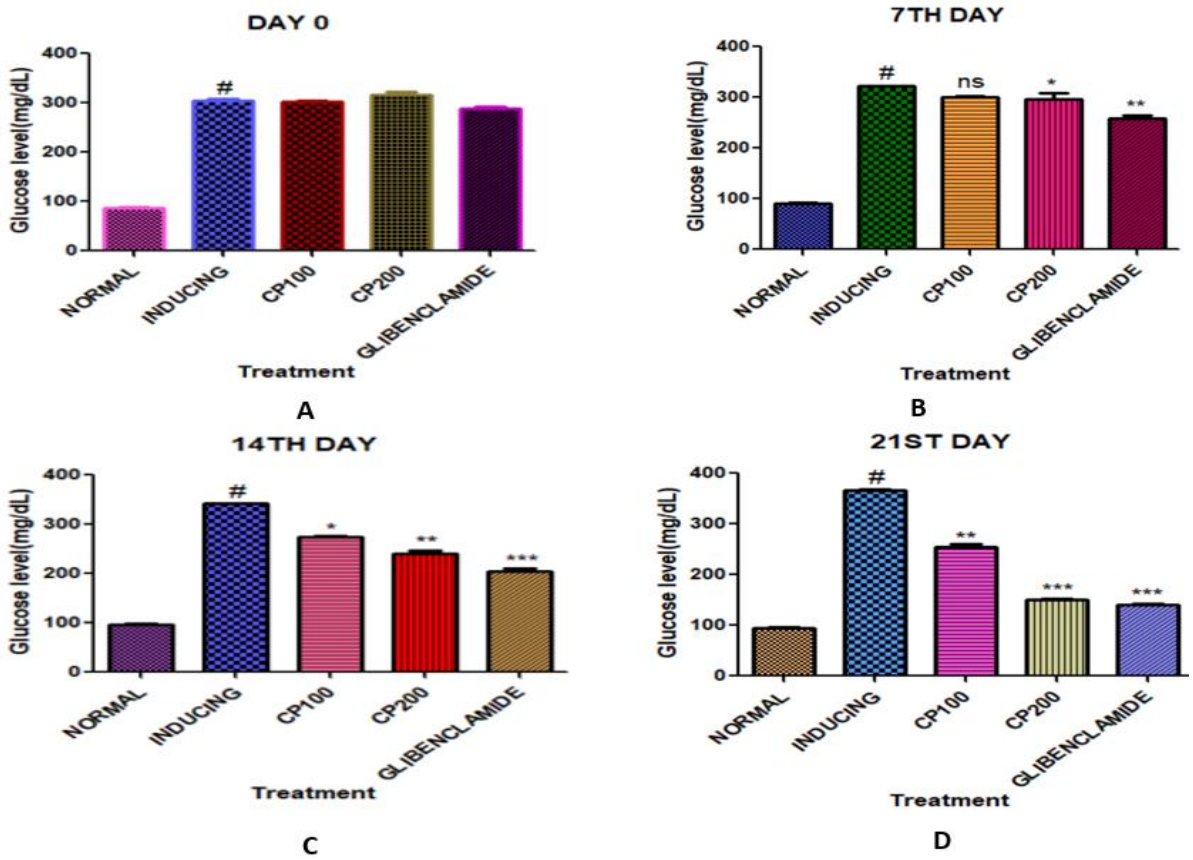
Each value represents Mean ± S.E.M., for n=6. * $p<0.05$, * * $p<0.01$, *** $p<0.001$ compared to diabetic control in OGTT in diabetic rats.

Table 5: Effect of CP on blood glucose level in Alloxan-induced diabetic rats

GROUP	0thday	7th day	14thday	21thday
Normal	87.2±1.655	90.0±1.732	97.0±1.844	94.2±2.083
Diabetic control	305.0±2.345#	321.4±1.03#	341.4±1.778#	365.6±3.187#
DM+CP [100mg/kg]	302.0±3.082	299.4±2.926ns	273.8±2.80*	254.4±5.046**
DM+CP [200mg/kg]	317.0±5.992	296.0±6.36*	240.6±5.501**	150.2±3.023***
DM+glibenclamide (2.5mg/kg)	288.4±3.311	259.2±5.571**	204.8±6.499***	139.4±3.415***

The CP 200 mg/kg group demonstrates a significant decrease in glucose levels on the 7th day ($p < 0.05$), with a notable decrease to 150.2 ± 3.023 mg/dL on the 21st day ($p < 0.001$), indicating a strong effect in regulating blood glucose. Similarly, the glibenclamide treatment showed significant reductions at the 7th day ($p < 0.01$), 14th day ($p < 0.001$), and 21st day ($p < 0.001$) with glucose levels declining to 139.4 ± 3.415 mg/dL.

Figure 3: Effect of CP on blood glucose levels in Alloxan-induced diabetic rats (A, B, C, D)



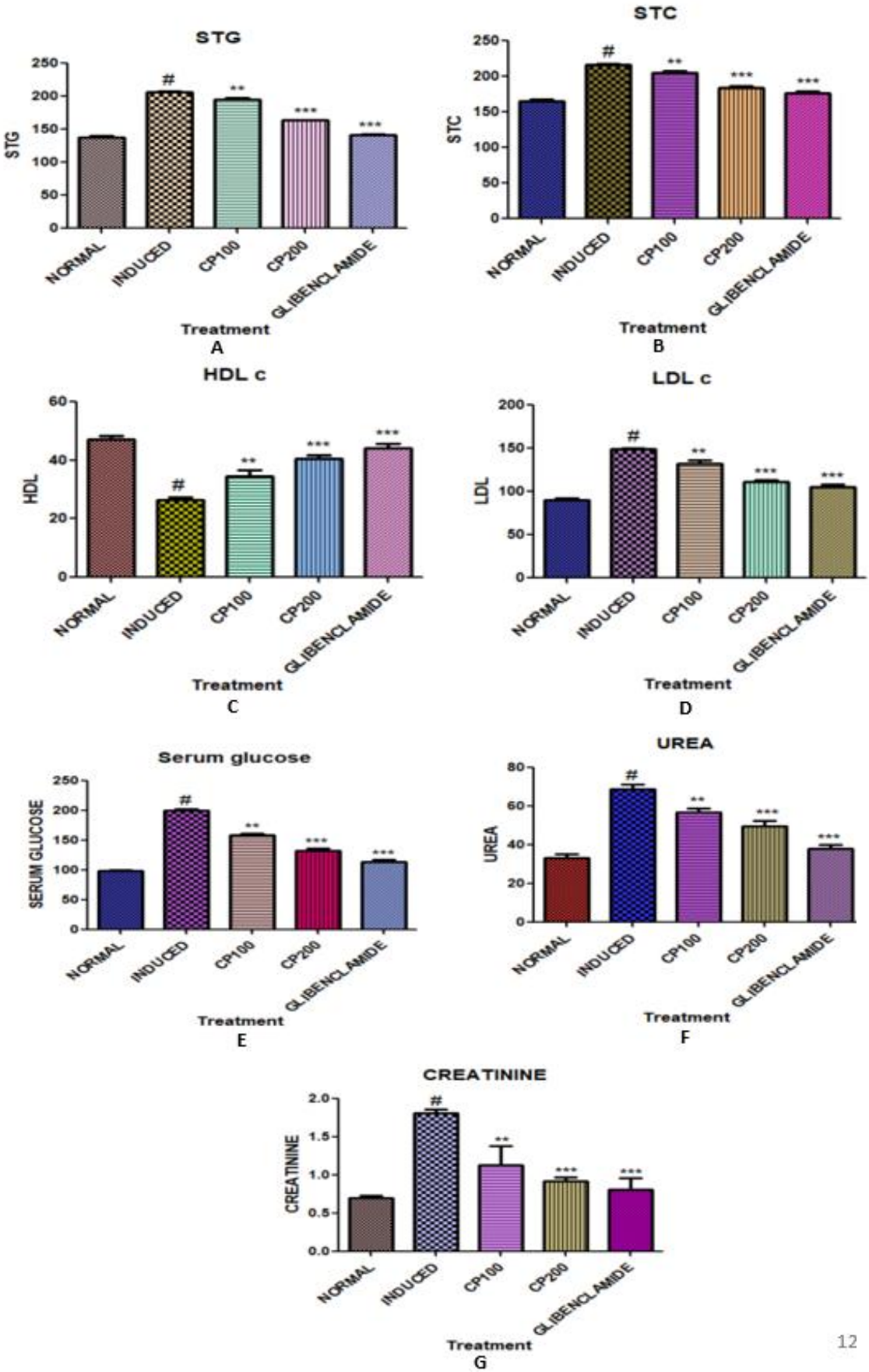
Each value represents Mean ± S.E.M., for n=6. *p<0.05, **p<0.01, ***p<0.001compared to diabetic control; #p<0.001compared to normal control animals.

LIPID PARAMETERS AND RENAL BIOMARKERS

Table 6: Effect of CP on Lipid parameters and renal biomarkers

Parameter	Normal Control	Diabetic Control	DM+CP (100mg/kg)	DM+CP (200mg/kg)	DM+Glibenclamide (2.5mg/kg)
STG (mg/dl)	137.7±2.319	206.3±1.593#	195.6±2.275**	163.4±1.058***	141.3±1.789***
STC (mg/dl)	165.3±1.886	216.3±1.138#	205.7±2.176**	184.5±1.512***	177.1±2.158***
HDL c(mg/dl)	47.30±1.134	26.36±1.030#	34.43±2.178**	40.47±1.174***	44.12±1.548***
LDL c(mg/dl)	27.54±0.4643	41.24±0.3228#	39.13±0.4544**	32.67±0.2123***	28.26±0.3579***
SERUM GLUCOSE	99.12±1.070	200.7±2.431#	159.0±2.455**	133.1±2.845***	114.4±2.868***
UREA	33.20±2.094	69.03±2.212#	56.79±2.142**	49.47±3.007***	38.02±2.191***
CREATININE	0.70±0.024	1.81±0.050#	1.133±0.244**	0.926±0.041***	0.815±0.1433***

Figure 4: Effect of CP on Lipid parameters and renal biomarkers (A, B, C, D, E, F, G)



Each bar represents the Mean ± S.E.M., for n=5. *p< 0.05; **p< 0.01; ***p < 0.001 compared with diabetic control group.

Serum Triglycerides (STG): The diabetic control group showed significantly ($p < 0.01$) elevated triglyceride levels at 206.3 ± 1.593 mg/dL compared to normal control animals. CP 100 mg/kg treated animals showed reduced triglyceride level 195.6 ± 2.275 mg/dL ($p < 0.01$), while the CP 200 mg/kg administered rats further significantly ($p < 0.001$) lowered triglycerides levels to 163.4 ± 1.058 mg/dL. Glibenclamide treatment also showed a significant ($p < 0.001$) reduction to 141.3 ± 1.789 mg/dL compared to diabetic control rats.

Serum Total Cholesterol (STC): The diabetic control group has total cholesterol levels of 216.3 ± 1.138 mg/dL which was significantly high ($p < 0.001$) compared to normal control rats. CP 100 mg/kg exhibited reduced total cholesterol to 205.7 ± 2.176 mg/dL ($p < 0.01$), while the CP 200 mg/kg dose further decreases ($p < 0.001$) it to 184.5 ± 1.512 mg/dL. Glibenclamide shows a similar effect, with significant ($p < 0.001$) reduction in total cholesterol at 177.1 ± 2.158 mg/dL.

High-Density Lipoprotein Cholesterol (HDL-c): The diabetic control group has significantly ($p < 0.001$) low HDL-c levels at 26.36 ± 1.030 mg/dL compared to normal control animals. CP 100 mg/kg treated rats showed significant ($p < 0.01$) increased HDL-c to 34.43 ± 2.178 mg/dL, and the CP 200 mg/kg treated animals showed significant increase ($p < 0.001$) to 40.47 ± 1.174 mg/dL ($p < 0.001$). Glibenclamide treatment results in an HDL- c level of 44.12 ± 1.548 mg/dL, indicating a strong ($p < 0.001$) improvement.

Low-Density Lipoprotein Cholesterol (LDL-c): The diabetic control group showed elevated levels of LDL-c at 41.24 ± 0.3228 mg/dL compared to normal control animals. CP 100 mg/kg lowers this to 39.67 ± 0.4544 mg/dL ($p < 0.01$), while the CP 200 mg/kg dose reduces it further to 32.67 ± 0.2123 mg/dL ($p < 0.001$). Glibenclamide also significantly ($p < 0.001$) reduces LDL-c to 28.26 ± 0.3579 mg/dL.

Serum glucose: The diabetic control group showed significantly ($p < 0.01$) elevated glucose levels at 200.7 ± 2.431 mg/dL compared to normal control animals. CP 100 mg/kg treated animals showed reduced to 159.0 ± 2.455 mg/dL ($p < 0.01$), while the CP 200 mg/kg administered rats further significantly ($p < 0.001$) lowered glucose levels to 133.1 ± 2.845 mg/dL. Glibenclamide treatment also showed a significant ($p < 0.001$) reduction to 114.4 ± 2.868 mg/dL compared to diabetic control rats.

Urea: The diabetic control group showed significantly ($p < 0.01$) elevated urea levels at 69.03 ± 2.212 mg/dL compared to normal control animals. CP 100 mg/kg treated animals showed reduced to 56.79 ± 2.142 mg/dL ($p < 0.01$), while the CP 200 mg/kg administered rats further significantly ($p < 0.001$) lowered urea levels to 49.47 ± 3.007 mg/dL. Glibenclamide treatment also showed a significant ($p < 0.001$) reduction to 38.02 ± 2.191 mg/dL compared to diabetic control rats.

Creatinine: The diabetic control group showed significantly ($p < 0.01$) elevated creatinine levels at 1.81 ± 0.050 mg/dL compared to normal control animals. CP 100 mg/kg treated animals showed reduced to 1.133 ± 0.244 mg/dL ($p < 0.01$), while the CP 200 mg/kg administered rats further significantly ($p < 0.001$) lowered creatinine levels to 0.926 ± 0.041 mg/dL. Glibenclamide treatment also showed a significant ($p < 0.001$) reduction to 0.815 ± 0.041 mg/dL compared to diabetic control rats.

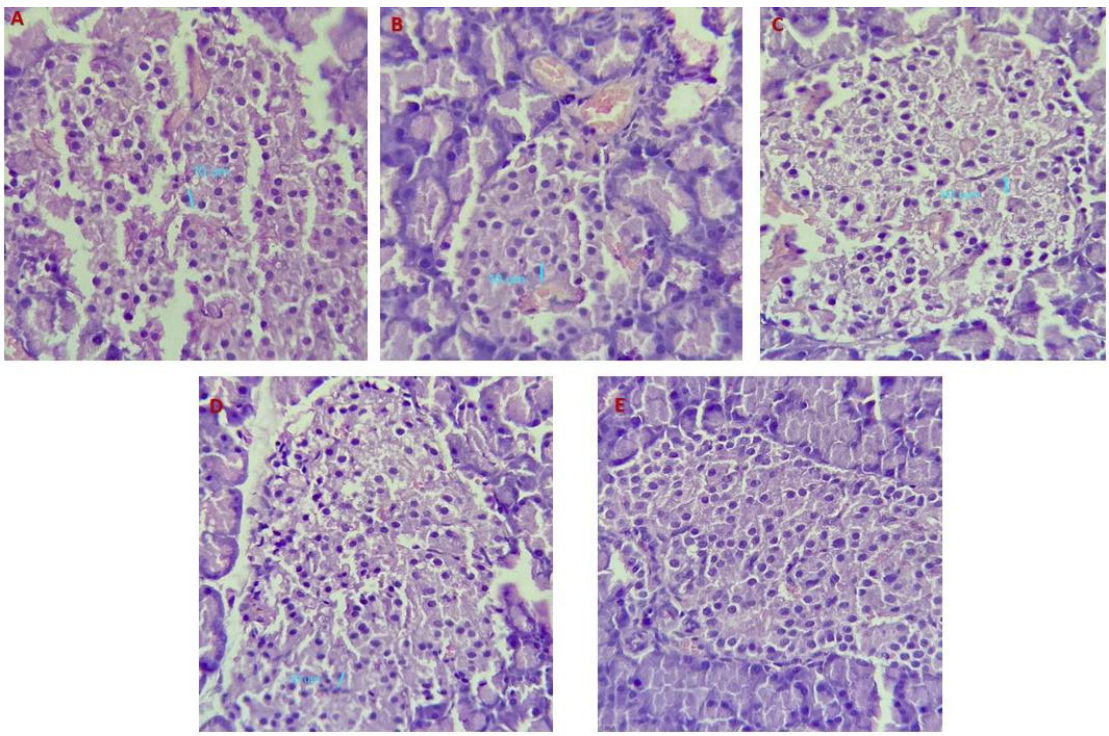


Figure 5: Effect of CP on histomorphological change in pancreas of different groups of animals [A] Normal control [B] Diabetic control [C] Diabetic + CP (100 mg/kg) [D] Diabetic + CP (200 mg/kg) [E] Diabetic + Glibenclamide (2.5mg/kg).

HISTOPATHOLOGICAL EXAMINATION

In the **Normal group**, pancreatic sections showed intact islets of Langerhans with well-arranged β-cells and normal acinar architecture without any pathological changes. The **Inducing group** exhibited severe degeneration and necrosis of β-cells, reduction in the size and number of islets, vacuolation, and infiltration of inflammatory cells, confirming alloxan-induced pancreatic damage and loss of insulin-secreting cells. The **Standard group** showed considerable protection, with restoration of islet size, regeneration of β-cells, and preservation of near-normal pancreatic histoarchitecture, although with mild alterations. The test group with a **Lower dose CP (100 mg/kg)** displayed partial protection, showing moderate regeneration of islets and reduced necrosis compared to the diabetic control. The **Higher dose CP (200 mg/kg)** treated group demonstrated significant regeneration of β-cells with near-normal islet morphology, minimal vacuolation, and better preservation of pancreatic tissue, comparable to the standard treatment.

DISCUSSION

Diabetes mellitus is a disorder in which the body tissues failed to utilize the glucose which leads to increased utilization of proteins responsible for reduction in body weight[15]The weight gain in CP-treated rats may result from improved glycemic control and protein synthesis, likely due to reduced hepatic gluconeogenesis and suppressed adipose tissue lipolysis. Abu-Odeh and Talib [16] suggested that the possible mechanism for body weight gain in plant extract-treated rats may be due to extra pancreatic action which might have contributed to the increased utilization of glucose by the tissues.

Diabetes is a metabolic disorder caused by impaired metabolism of carbohydrates, proteins, and lipids predisposing to hyperglycemia[17]. Glycemic control is the main target of the treatment to prevent micro- and macrovascular and neurological complications of diabetes[18].

Research shows that hypoglycemic medicinal plants work by enhancing insulin sensitivity, boosting insulin secretion, and promoting β-cell regeneration in the pancreas[19]. Several authors reported that the presence of flavonoids, steroids, terpenoids, and phenols is responsible for antidiabetic activity. Flavonoids have also been known to regenerate the damaged beta cells in alloxan- induced diabetic rats and act as insulin secretagogues[20].

In this study, the significant reduction in blood glucose levels observed in the CP-treated groups may be attributed to the regeneration of pancreatic β-cells, resulting in enhanced insulin secretion and improved glycemic control. Previous study and in our phytochemical study showed the presence of alkaloids and flavonoids in the extract[21].

It has been shown that flavonoids possess antidiabetic activity in alloxan-induced diabetic rats through regeneration of pancreatic islets which increases insulin secretion[22]. This histological evidence may also account for the hypoglycemic activity of the CP. Biologically active, naturally occurring phytochemical compounds found in plants provide health benefit for humans[23].CP's antidiabetic and hypolipidemic effects are likely due to its polyphenols, along with antioxidant and anti-hyperlipidemic properties beneficial for diabetes.

The endocrine capability of pancreas is determined by apoptosis, replication, and neogenesis of beta cells of islets of Langerhans[24]. Oxidative stress plays an important role in beta cell dysfunction and apoptosis[25].

In this context, the protective effect of some phytochemicals on pancreas has been found to be mediated through their antioxidant activity[26]. Some phytochemicals promote the growth and specialization of progenitor cells that aid in β-cell regeneration. Many plants contain natural antioxidants like phenols and flavonoids, while tannins may support pancreatic repair through anti-inflammatory effects[27].The phytochemicals and amino acids in the herbal plants are associated with regeneration of β-cells in diabetic rats[28].

CONCLUSION

The findings in the present study indicated that the methanolic extract of *Caesalpinia pulcherrima (Linn) Swartz* leaves exhibited anti-diabetic activity against alloxan induced diabetes mellitus via up-regulation of the secretion and sensitivity to insulin, improvement of glucose homeostasis, antioxidant mechanism, and restoration of pancreatic histoarchitecture. The presence of tannins, saponins, flavonoids and phenolics might have conferred the desired anti-diabetic activity.

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