

Research Article

Evaluation of the Anti-diabetic Activity of Ethanolic Extract of *Citrus maxima* Stem Bark

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ABSTRACT

The objective of present study is to evaluate the antidiabetic activity of ethanolic extract of stem bark of *Citrus maxima*. The term diabetes mellitus describes a metabolic disorder of multiple aetiology characterized by chronic hyperglycaemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both. A search for appropriate antidiabetic agent has focused on plants used in traditional medicine because natural products maybe a better option than currently used allopathic drugs due to the freedom from side effects.¹ *In-vivo* hypoglycemic activity of the *Citrus maxima* fruits and fruit peel have been already documented in the literature². This study was under taken to evaluate the Antidiabetic activity of *Citrus maxima* stem bark extract using Alloxan and Streptozotocin induced diabetes in Wistar rats. The results of the present study indicated that *Citrus maxima* stem bark extract possesses significant antidiabetic activity against streptozotocin and alloxan induced diabetic rats. Stem bark extract of the title plant possesses dose dependant antidiabetic activity when compared with reference standard Glibenclamide. A significant decrease in blood glucose level was observed with the two selected doses, 200mg/kg and 400mg/kg of *Citrus maxima* stem bark extract hence can be used in diabetes. Antidiabetic activity of *Citrus maxima* at 400 mg/kg was found to be more effective than 200 mg/kg.

Keywords: Hyperglycaemia, *Citrus maxima*, Alloxan, Streptozotocin, Glibenclamide.

INTRODUCTION

Diabetes Mellitus³ is a syndrome of impaired carbohydrate, fat and protein metabolism caused by either lack of insulin secretion or decreased sensitivity of the tissue to insulin. Diabetes is derived from the Greek word meaning syphon, to signify the copious urine production in individuals with this affliction. Diabetes has been recognized for at least 2000 years. Several distinct types of Diabetes Mellitus are caused by a complex interaction of genetics and environmental factors.

Several classes of allopathic drugs namely sulphonylureas, biguanides, thiazolidinones, alpha glucosidase inhibitors and semi synthetic insulin are extensively used to control the hyperglycemia. These drugs exert different modes of action to reduce the elevated blood glucose, but none of them were found to be effective in providing complete glycaemic control in diabetic patients, moreover these drugs also exert their individual adverse effects such as pregnancy related complications and hypoglycemic episodes

when administered to the diabetic patients⁴. Hence there is a need for a antidiabetic drugs/formulation that can provide optimal glycaemic control without producing unwanted side effects in the host system.⁵

From ancient times, the herbs have been extensively used in the therapy of several diseases. A search for appropriate antidiabetic agent has focused on plants used in traditional medicine because natural products maybe a better option than currently used allopathic drugs due to the freedom from side effects.⁶ Many herbal products have been described for the treatment of diabetes mellitus in literature⁷. Moreover, WHO also recommends the inclusion of traditional medicine such as herbs or herbal products in the primary health care level.⁸ Although, several plant products are traditionally used to treat the hyperglycemia related complications, still many agents are poorly studied in the literature⁹.

Citrus maxima, the pomelo in the Rutaceae (citrus family). It is a medium-

sized tree but the largest of all Citrus species, with large leaves, flowers, and fruits. The species is native to southern China and Malaysia, Taiwan and southernmost Japan, southern India, Malaya, Indonesia, New Guinea and Tahiti, and is now cultivated in many tropical and semi-tropical countries for its large fruits. Like other citrus fruits, pomelos are high in vitamin C. They are generally eaten as a fresh fruit, and they store well. They have long been popular in Asia, especially China, Indonesia, and Thailand, but are increasingly found in specialty markets in the U.S. as well. The juice is also used in various beverages, and the peel may be candied. Traditional medicinal uses of the fruit include treatment of coughs, fevers, and gastrointestinal disorders¹⁰.



Citrus maxima was cited for its various medicinal properties, especially Analgesic, Anti-inflammatory¹¹, Anti-bacterial¹², Antioxidant^{13,15}, Hepatoprotective¹⁴, Antidiabetic^{16,17,20}, Anti-depressant¹⁸, Antitumour^{19,21} and Antihyperlipidemic²⁰ properties.

In-vivo hypoglycemic activity of the *Citrus maxima* fruits and fruit peel have been already documented in the literature²⁰. However, studies on Antidiabetic potential of stem bark of the title plant on Alloxan and streptozotocin induced diabetes in rat has not been investigated so far. Hence, the present investigation is undertaken.

MATERIALS AND METHODS

Collection and authentication of plant material

The fresh stem bark of *Citrus maxima* used for the present studies were collected from Malappuram, Kerala, in June 2013. It was authenticated by Mr. Prabu Kumar, Scientist

Kottakkal Aryavaidya Sala, Kerala.. The Stem bark were dried under shade. The dried Stem bark were pulverized separately into coarse powder by a mechanical grinder and were used for extraction.

Preparation of Ethanolic Extract

The powdered material (150 g) was packed in Soxhlet extractor and extracted using ethanol as solvent. The temperature was maintained on an electric heating mantle with thermostat control. Appearance of colourless solvent in the siphon tube was taken as the termination of extraction. The extract was concentrated to syrupy consistency by using rotary flash evaporator. The concentrated extract was then air dried at room temperature, weighed and percentage yield was calculated and stored in air tight container in 2–8°C until used.

Experimental animals

Healthy Wistar albino rats (150–200 g) of either sex were used for the experiment and were procured from the animal house of Srinivas College of Pharmacy, Mangalore. They were maintained under standard conditions (temperature 22 ±2°C, relative humidity 60 ± 5% and 12 h light/dark cycle). The animals were housed in sanitized polypropylene cages containing paddy husk as bedding. They had free access to standard pellet diet and water *ad libitum*. The Institutional Animal Ethics Committee approved the experimental protocol (Approval No. SCP/CPCSEA/P12/F150/2011). All the animals received human care according to the criteria outlined in the "Guide for the Care and Use of Laboratory Animals" prepared by the "National Academy of Sciences" and published by the "National Institute of Health". The animals were acclimatized for at least one week before use.

Pharmacological activities

1. Acute oral toxicity
2. Antidiabetic activity

Acute toxicity study²².

Acute oral toxicity study was performed as per OECD-425 guidelines (acute toxic class method). Wistar albino 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 that the extracts were administered orally at the dose level of 2000mg/kg body weight by intragastric tube and kept under close observation for 24 hrs after administering the extract, and then they were observed daily for 3 days for any change in

general behavior and or other physical activities. After 24 h, there were no died animals representing the safety action of all extracts. Method of CPCSEA was adopted for toxicity studies, 1/10th and 1/5th LD50 cut off value of the extract were selected as screening dose.

Anti-diabetic Activity

Alloxan induced anti-diabetic activity^{23,24}

Fasting blood glucose was determined after depriving food for 16 h with free access to drinking water. Hyperglycemia was induced by single i.p injection of 100 mg/kg of Alloxan monohydrate in normal saline. After 2 days of Alloxan injection, the hyperglycemic rats (glucose level > 200 mg/dl) were separated and divided into four groups consisting of six rats in each group for the anti-diabetic study. The treatment (p.o) was started from the same day except diabetic control groups. The animals had free access to feed and water *ad libitum*.

Experimental design

Animals will be randomly divided into 5 groups of 6 each. The different groups will be assigned as follows

- Group I: Vehicle control (normal saline).
- Group II: Diabetic control (Alloxan 100mg/Kg).
- Group III: Diabetic + Glibenclamide (1mg/Kg)
- Group IV: Diabetic + Citrus maxima (200mg/kg)
- Group V: Diabetic + Citrus maxima (400mg/kg)

Streptozotocin induced anti-diabetic activity^{25,26}

Fasting blood glucose was determined after depriving food for 16 h with free access to drinking water. Hyperglycemia was induced by single i.p injection of 65 mg/kg of STZ in citrate buffer, freshly prepared and injected within 5 minute of preparation to prevent degradation. After administration of STZ the animals had free access to feed and water *ad libitum*. The development of hyperglycemia in rats was confirmed by fasting blood glucose estimation 48 h post STZ injection wherein animal were fasted overnight again for blood collection from retro orbital sinus. The rats with fasting blood glucose level of above 200 mg/dl at 48 h after STZ injection were considered diabetic and included in the study.

Experimental design

Animals will be randomly divided into 5 groups of 6 each and assigned as below.

- Group I: Vehicle control (Citrate buffer).
- Group II: Diabetic control (Streptozotocin 65mg/Kg).
- Group III: Diabetic + Glibenclamide (1mg/Kg)

Group IV: Diabetic + Citrus maxima (200mg/kg)

Group V: Diabetic + Citrus maxima (400mg/kg)

Collection of blood and serum samples

The above treatment was carried out in each group of animals for both models for 21 days. Fasting blood glucose was measured using select simple single touch glucometer. Blood samples were withdrawn under mild anesthesia from retro orbital sinus of the overnight fasted animals on 1st, 7th, 14th, and 21st day. On 21st day the blood was collected for biochemical estimations by retro orbital puncture. The serum was obtained by centrifuging the blood samples at 3000 rpm for 10 min and they were used for estimation of SGPT, SGOT by using a corresponding kit from Agappe Diagnostics Pvt. Ltd and the intensity of the coloured complex formed after treating with these reagents were estimated in semi-auto analyzer.

Oral glucose tolerance test²⁷

The oral glucose tolerance test was performed in overnight fasted normal rats. Rats were divided into three groups (each group containing six animals). The first group was kept as vehicle control and received 1 ml of normal saline, the experimental group II was received standard drug Glibenclamide (1 mg/kg) and group III was received test drug (*Citrus maxima*). After 30 minutes glucose (2 g/kg) was fed to all groups. Blood was withdrawn from the retro-orbital sinus just prior to the glucose administration and at 30, 60, 120, 180 and 240 minutes after glucose loading and glucose levels were measured.

The parameters studied were as follows

- Biochemical parameters such as
 - i. Fasting blood glucose
 - ii. Serum glutamic pyruvate transaminase (SGPT)
 - iii. Serum glutamic oxaloacetate transaminase (SGOT)
- Morphological parameter includes
 - i. Body weight

Estimation of SGPT (UV- Kinetic method)²⁸

Principle

SGPT catalyses the transfer of amino group from L-Alanine to 2-oxoglutarate with the formation of pyruvate and L-glutamate. The pyruvate so formed is allowed to react with NADH to produce L-lactate. The rate of this reaction is monitored by an indicator reaction coupled with LDL in the presence of NADH (nicotinamide adenine dinucleotide). The

oxidation of NADH in this reaction was measured as a decreasing in the absorbance of NADH at 340 nm, which is proportional to SGPT activity.

Procedure

Pipette	Sample (μ l)
Working reagent	1000
Sample	100

Mix well and incubate at 37°C for 5 min. Aspirate blank followed by standard and tests the measure the absorbance of the sample and standard against blank at 340 nm using Semi-auto analyzer.

Formula

$$\text{SGPT (U/L)} = \text{Absorbance} \times 1746 \text{ (Factor)}$$

Estimation of SGOT (UV- kinetic method)²⁹

Principle

SGOT catalyses the transfer of amino group from L- Aspartate to 2-oxo glutarate with the formation of oxaloacetate and L-glutamate. The rate of this reaction is monitored by an indicator reaction coupled with malate dehydrogenase (MDL) in which the oxaloacetate formed is converted to malate ion in the presence of NADH (nicotinamide adenine dinucleotide). The oxidation of NADH in this reaction was measured as a decreasing in the absorbance of NADH at 340 nm, which is proportional to SGOT activity.

Procedure

Pipette	Sample (μ l)
Working reagent	1000
Sample	100

Mix well and incubate at 37°C for 5 min. Aspirate blank followed by standard and tests the measure the absorbance of the sample and standard against blank at 340 nm using Semi-auto analyzer.

Formula

$$\text{SGOT (U/L)} = \text{Absorbance} \times 1746 \text{ (Factor)}$$

Statistical analysis

Results of biochemical estimation were reported as mean \pm S.E.M. The total variation present in a data was analyzed by one way analysis of variance (ANOVA). P value less than 0.05 was considered as statistically significant.

RESULTS

Percentage yield

Percentage yield of crude ethanolic extract of *Citrus maxima* stem bark using Hot percolation method was found to be 10.2 % and Brownish black colour.

Preliminary phytochemical screening of extract

The ethanolic extract of *Citrus maxima* stem bark was subjected to screening for its phytochemical constituents and ethanolic extracts showed the presence of flavonoids, tannins, alkaloids, glycosides and carbohydrates.

Acute toxicity studies of ethanolic extract

The acute toxicity of ethanolic extracts of *Citrus maxima* was carried out as per OECD-425 guidelines for safe dose administration to animals. The results of acute toxicity study revealed that LD₅₀ values of extract were high and apparently showed the safety of the extract. The treatment of rats with ethanolic extract of *Citrus maxima* did not change the autonomic or behavioral responses among rats. The zero percent mortality was found at the doses of 2000 mg/kg. Based on the results, 1/10th and 1/5th of 2000 mg/kg was taken as low dose (200 mg/kg) and high dose (400 mg/kg) as therapeutic dose of the present investigation.

Anti-diabetic Activity

Alloxan induced anti-diabetic activity

Fasting blood glucose (FBG) level was within the range of 80-95 mg/dl in all the groups prior to diabetic induction. Treatment with Alloxan in normal saline (100 mg/kg, i.p) had increased the FBG level above 250 mg/dl after 42 h. Treatment with ethanolic extract of *Citrus maxima* stem bark significantly normalized the elevated blood glucose level as shown in Table 1.

Streptozotocin induced anti-diabetic activity

Fasting blood glucose (FBG) level was within the range of 80-90 mg/dl in all the groups prior to STZ administration. Treatment with STZ in normal saline (65 mg/kg, i.p) had increased the FBG level above 200 mg/dl after 72hrs. Treatment with ethanolic extract of *Citrus maxima* stem bark significantly normalized the elevated blood glucose level as shown in Table 2.

Oral glucose tolerance test (OGTT) in normal rats

Treatment with Ethanolic extract of *Citrus maxima* stem bark showed significant reduction in the blood glucose level after glucose loading as compared to normal control as shown in Table 3.

Effect on body weight

Alloxan induced diabetic rats

Body weight of animals in all groups was recorded at 0, 7th, 15th and 21st day. Highest change (decrease) in body weight during study period was found to be in diabetic control group. Glibenclamide and *Citrus maxima* stem bark extract treated groups showed increase in body weight as compared to diabetic control group. (Table 4)

STZ induced diabetic rats

Body weight of animals in all groups was recorded at 0, 7th, 15th and 21st day. Highest change (decrease) in body weight during study period was found to be in diabetic control group. Glibenclamide and *Citrus maxima* stem bark extract treated groups showed increase in body weight as compared to diabetic control group. (Table 5).

Serum biomarkers

After 21 days of experiment, serum biomarkers such as SGPT and SGOT level were significantly elevated in diabetic control group. In animals treated with Glibenclamide and *Citrus maxima* stem bark extract, SGPT and SGOT levels were decreased significantly ($p < 0.001$, $p < 0.01$ respectively) as compared to the diabetic control. (Table 6).

DISCUSSION

Diabetes mellitus is chronic disorder caused by partial or complete insulin deficiency. This causes abnormal metabolism of glucose, protein and lipid leads to acute and chronic complications. The major complications are the premature and extensive atherosclerosis involving renal, peripheral and cardiovascular vessels. Disorder is more likely to increase risk for coronary heart disease because of alteration in serum lipid profile.

In present study, treatment with *Citrus maxima* stem bark ethanolic extract in alloxan and streptozotocin treated rats produced significant decrease in blood glucose level. The hypoglycemic effect may be due to increased secretion of insulin from β cells of pancreas i.e. pancreatotrophic action³⁰ or due to regeneration of pancreatic cells that were partially destroyed by alloxan.

The preliminary phytochemical screening of the plant showed the presence of flavonoids and tannins in ethanolic extract. It is well known that flavonoids and tannins possess antidiabetic property.³¹

Alloxan, a β cytotoxic induces chemical diabetes in wide variety of animal species by damaging the insulin secreting cells of pancreas³². Literature survey indicates that alloxan treated rats are hyperglycemic³³. Alloxan (100 mg/kg) produces partial destruction of pancreatic β cells and these animals may have surviving β cells and regeneration of β cells is possible.³³

STZ has been shown to produce free radicals in the body, which specifically cut DNA chains in the pancreatic beta cells, resulting in disorder of the function of the pancreatic beta cells and at a later phase, destruction of the beta cells by necrosis. Streptozotocin injection induces over-production (excessive hepatic glycogenolysis and gluconeogenesis) and decreased utilization of glucose by the tissues are the fundamental basis of hyperglycemia in diabetes mellitus³⁴.

Destruction of beta cells results in elevation of blood glucose level³⁵. Alloxan and STZ induced diabetic group that was treated with low dose (200mg/kg) and high dose (400mg/kg) of *Citrus maxima* ethanolic stem bark extract and also the Glibenclamide treated group showed significant decrease in Alloxan and STZ induced elevation in plasma glucose. The non diabetic group treated with high dose (400mg/kg) of *Citrus maxima* ethanolic stem bark extract showed significant decrease in plasma glucose when compared with vehicle control.

The loss of body weight and increase in food and fluid intake of diabetic rats as compared to that of control rats could be due to emaciation of skeletal muscle, dehydration and catabolism of fats and proteins^{36, 37, 38}. Decrease in body weight was found in diabetic control group. Data of present study shows that treatment with *Citrus maxima* stem bark extract prevents loss of body weight in diabetic condition significantly, which may be due to its protective effect in controlling muscle wasting i.e. reversal of gluconeogenesis and may also be due to the improvement in insulin secretion and glycaemic control³⁹.

The diabetes complication such as increased gluconeogenesis and ketogenesis may be due to elevated transaminase activity. Elevation of biomarker enzymes such as SGPT and SGOT was observed in diabetic rats in present study, which indicates the hepatic damage. Elevated enzyme activity restored by ECMS treatment with both 200mg/kg and 400mg/kg, shows

dose dependent activity which signifies anti diabetic activity.

The administration of *Citrus maxima* stem bark extract to the diabetic animals decreased the elevated serum biomarkers levels. Earlier studies indicated that herbal drugs can reduce the increased biomarker level in diabetic condition and the mechanism is suggested is due to the antioxidant potential⁴⁰.

CONCLUSION

Many herbal medicines have been recommended for the treatment of diabetes. Phytochemical investigations of these herbal drugs have shown antidiabetic activity which reveals the presences of flavonoids, sterols, polyphenols and tannins as bioactive principles. Our data suggest that the 80% aqueous alcoholic extract of stem bark of *Citrus maxima* possess potential antidiabetic activity as it lowers serum glucose level and moderately increases glucose tolerance. Intraperitoneal administration of Alloxan and STZ produced cardinal symptoms such as hyperglycemia, loss of body weight. Also

impaired lipid and glucose metabolism and altered kidney function, increase in serum biomarkers (liver damage).

A significant decrease in blood glucose level was observed with the two selected doses, 200mg/kg and 400mg/kg of *Citrus maxima* stem bark extract hence can be used in diabetes. Antidiabetic activity of *Citrus maxima* at 400 mg/kg was found to be more effective than 200 mg/kg.

In the present study, the administration of ethanolic extract of stem bark of *Citrus maxima* shows a significant antidiabetic effects in Alloxan and STZ induced diabetic rats. However Further studies are needed to be isolate the active constituents of *Citrus maxima* and also to be evaluate the exact mechanism of action for the antidiabetic activity.

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Table 1: Serum glucose in alloxan induced diabetic rats

GROUPS	Blood glucose level (mg/dl)				
	Before diabetic induction	Day 0	Day 7	Day 14	Day 21
Normal control	85.12±2.38	84.85±1.86	87.05±0.92	87.55±1.66	86.65±2.13
Diabetic control	87.65±4.36	250.54±3.62	254.62±4.36#	257.09±5.65#	266.98±6.32#
Standard Glibenclamide (5mg/kg)	88.31±2.32	261.16±2.65	201.01±6.4***	160.87±2.98***	134.65±3.54***
Low dose <i>C.maxima</i> (200mg/kg)	86.16±4.78	255.33±7.65	235.67±5.23*	195.74±6.29**	158.60±5.76**
High dose <i>C.maxima</i> (400mg/kg)	88.13±3.85	244.723.61	196.82 ±6.54**	164.36 ±9.3***	142.80 ±8.96***

Values are mean ± SEM (n=6) one way ANOVA followed by Dunette's t test. Where,

represents the comparison, * represents significant at $p < 0.05$, ** represents highly significant at $p < 0.01$ and *** represents very significant at $p < 0.001$.

Table 2: Serum glucose in STZ induced diabetic rats

GROUPS	Blood glucose level (mg/dl)				
	Before diabetic induction	Day 0	Day 7	Day 14	Day 21
Normal control	87.54±1.38	90.88.10±1.86	89.92±1.92	89.37±2.56	90.25±3.16
Diabetic control	90.01±4.58	288.41±2.26	293.11±5.367#	310.87±4.56#	318.91±5.23#
Standard Glibenclamide (5mg/kg)	89.44±1.132	280.87±2.56	241.78±6.54***	170.59±4.89***	130.36±3.45***
Low dose <i>C.maxima</i> (200mg/kg)	88.22±4.67	300.08±7.56	280.23±4.32*	225.25±5.92**	170.65±4.67**
High dose <i>C.maxima</i> (400mg/kg)	87.35±6.45	254.98 ±5. 19	225.13±4.13**	187.21 ± 3.15***	139.01±9.41***

Values are mean ± SEM (n=6) one way ANOVA followed by Dunette's t test. Where, # represents the comparison, * represents significant at $p < 0.05$, ** represents highly significant at $p < 0.01$ and *** represents very significant at $p < 0.001$.

Table 3: Blood glucose levels on OGTT in normal rats

GROUPS	Blood glucose level (mg/dl)				
	0 min	30 min	60 min	120 min	240 min
Normal	84.80±1.38	145.87±1.86	125.64±2.92	110.77±2.66	87.48±4.12
Standard Glibenclamide (5mg/kg)	86.76±2.58	120.98±2.26**	95.12±4.67**	88.54±5.46**	81.34±4.32**
Low dose <i>C.maxima</i> (200mg/kg)	89.98±1.12	115.65±2.61*	107.25±5.48*	100.84±4.65*	92.52±3.55*
High dose <i>C.maxima</i> (400mg/kg)	88.96±4.87	118.25±5.57**	105.25±2.54**	97.14±3.82**	89.71±2.65**

Values are mean ± SEM (n=6) one way ANOVA followed by Dunette's t test. Where, # represents the comparison, * represents significant at $p < 0.05$, ** represents highly significant at $p < 0.01$.

Table 4: Body weight in alloxan induced diabetic rats

GROUPS	BODY WEIGHT (Grams)			
	Day 0	Day 7	Day 14	Day 21
Normal Control	201.50 ± 2.75	203.10 ± 2.78	205.60 ± 2.80	209.90 ± 2.86
Diabetic Control	203.50 ± 2.89	172.00 ± 2.59#	158.52 ± 2.51#	145.67 ± 1.72#
Standard Glibenclamide (5mg/kg)	206.50 ± 2.84	203.00 ± 2.64***	201.50 ± 2.02***	205.45 ± 1.90***
Low dose <i>C.maxima</i> (200mg/kg)	205.50 ± 2.39	189.00 ± 2.15*	184.34 ± 1.89*	187.50 ± 1.24*
High dose <i>C.maxima</i> (400mg/kg)	206.55 ± 2.45	200.00 ± 2.07**	202.00 ± 1.69**	203.00 ± 1.50***

Values are mean ± SEM (n=6) one way ANOVA followed by Dunette's test. Where, # represents the comparison, * represents significant at $p < 0.05$, ** represents highly significant at $p < 0.01$ and *** represents very significant at $p < 0.001$.

Table 5: Body weight in STZ induced diabetic rats

GROUPS	BODY WEIGHT (Grams)			
	Day 0	Day 7	Day 14	Day 21
Normal Control	185.33 ± 2.53	192 ± 4.31	202.00 ± 6.84	210.50 ± 9.79
Diabetic Control	190.67 ± 3.72	175 ± 3.41#	163.50 ± 0.99#	145 ± 1.59#
Standard Glibenclamide (5mg/kg)	205.50 ± 1.84	196.00 ± 3.64***	195.50 ± 4.02***	200.00 ± 3.90***
Low dose <i>C.maxima</i> (200mg/kg)	190.83 ± 1.30	177 ± 2.90*	179.50 ± 4.22*	181.67 ± 3.46**
High dose <i>C.maxima</i> (400mg/kg)	201.50 ± 6.45	186.50 ± 4.07**	190.10 ± 3.69**	195.25 ± 2.50***

Values are mean ± SEM (n=6) one way ANOVA followed by Dunette's t test. Where, # represents the comparison, * represents significant at $p < 0.05$, ** represents highly significant at $p < 0.01$ and *** represents very significant at $p < 0.001$.

Table 6: SGPT and SGOT levels in diabetic rats

Group	Alloxan		STZ	
	SGPT	SGOT	SGPT	SGOT
Normal control	55.12±1.28	56.98±1.45	58.73±2.65	60.13±3.75
Diabetic control	101.43±1.95#	112.48±1.65#	109.31±2.38#	111.92±1.05#
Standard Glibenclamide	70.78±1.65***	68.59±2.25***	65.23±3.54***	69.50±1.95***
Low dose <i>C.maxima</i> (200mg/kg)	98.45±2.65*	95.34±2.85*	91.80±2.11*	86.94±1.69*
High dose <i>C.maxima</i> 400mg	85.46±2.47**	77.18±2.39**	82.57±5.45**	78.65±3.12**

Values are mean ± SEM (n=6 except in control) one way ANOVA followed by Dunette's t test. Where, # represents the comparison, * represents significant at $p < 0.05$, ** represents highly significant at $p < 0.01$, *** represents very significant at $p < 0.001$.

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