Print ISSN: 2319-2003 | Online ISSN: 2279-0780

IJBCP International Journal of Basic & Clinical Pharmacology

DOI: http://dx.doi.org/10.18203/2319-2003.ijbcp20175671

Original Research Article

Evaluation of antihyperglycemic activities of Bangladeshi medicinal plant *Cinnamomum tamala* Leaf extracts in alloxan treated Albino Rats

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Received: 07 November 2017
Accepted: 28 November 2017

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ABSTRACT

Background: Diabetic mellitus is a multifactorial disorder associated with its devastating consequences has assumed epidemic proportion in Bangladesh.
Methods: The study evaluates the anti-hyperglycemic activity of the aqueous extracts of *C. tamala* (CTLEt) leaves in blood glucose of albino rats. Type II diabetes mellitus was induced by injecting alloxan at the concentration of 100mg/kg body weight in male albino rats. The diabetic rats were administered orally with aqueous CTLEt at the amount of 1.0ml, 1.5ml and 2.0ml with lab diet and glibenclamide (5mg/kg of body weight). Then blood glucose levels were estimated in all groups after 2 hours, 4 hours, 6 hours, 12 hours and 18 hours of the treatment with CTLEt and a known antidiabetic drug glibenclamide.
Results: A comparison was made between the action of CTLEt and glibenclamide. Blood glucose levels of the CTLEt on 18th hours of the study were 8.6 to 5.1mmol/L (1ml CTLEt with lab diet), 10.4 to 4.9mmol/L (1.5ml CTLEt with lab diet), 14.7 to 4.3mmol/L (2.0ml CTLEt with lab diet) in comparison of diabetic control (9.5 to 8.5, 8.7 to 7.8, 7.7 to 7.1mmol/L) and glibenclamide (13.9 to 6.5, 16.3 to 6.1, 9.5 to 5.1mmol/L). Among the sample level, the 2.0ml CTLEt showed a higher efficiency of hypoglycemic effect on alloxan induced diabetic rats.
Conclusions: Till date, there is no specific experimental work in Bangladesh about the evolution of antidiabetic activity of *C. tamala* plant in animal model. Further studies should be undertaken to find out the molecular mechanism of the leaf powder of *C. tamala* medicinal plant.

Keywords: Alloxan, Anti-hyperglycemic activity, *Cinnamomum tamala*

INTRODUCTION

Diabetes is a global public health problem associated with devastating consequences and has assumed epidemic proportion in developing countries of the world.[1] Diabetes mellitus is known as a non-communicable diseases resulting by decreased in insulin secretion, and impaired insulin action.[2] *C. tamala* is known as evergreen tropical tree, belonging to the Lauraceae family which is mainly used as flavoring agents in foods and is widely used in pharmaceutical preparations because of its hypoglycemic, stimulant and carminative properties. It grows throughout Bangladesh but is cultivated more in southern regions as a spice as well as for its medicinal value.[3] The leaves are carminative, stimulant, diuretic, diaphoretic, lactagogue, deobstruent and aromatic.[4] The leaves of this plant are used as spice having clove like taste and pepper like odor.[5] Leaves of *C. tamala* (Tejpata) also yield an essential oil in distillation. The essential oil of the leaves is called 'Tejpata oil' which is medicinally used as carminative, anti-flatulent, diuretic, and in cardiac disorders.[6] Previously, various researchers reported its phytochemical and pharmacological values by using standard experimental methods. For example, leaves of this plant are effective in diabetic rats have antioxidants as well as have hypoglycemic anti-inflammatory and immunomodulation properties.[7-10] Recent studies shows that the leaf extracts

of the plant have antidiabetic and antioxidant activities in streptozotocin (stz) treated diabetic rats and the bark was reported to have anti-diabetic activity by using α-amylase inhibition assay.[11,12] The present study focuses on the antidiabetic activities of the leaf extracts of *C. tamala* which are usually used in South-Asian cooking and sample was collected locally.

METHODS

C. tamala was collected from Tangail district in the central region of Bangladesh during January 2017. It was identified by Bangladesh national Herbarium Center (Acc. No. 43405) and the voucher specimen was deposited to the herbarium center Bangladesh. This study was undertaken in the laboratory of Biotechnology and Genetic Engineering Department, Mawlana Bhashani Science and Technology University, Santosh, Tangail, Bangladesh.

Preparation of plant extract

Leaves of *C. tamala* were extracted separately with 1.5 L of water by the method of continuous hot extraction at 60°C for 6 h and evaporated. These were designated as CTLEt. The residual extract was dissolved in water and used in the study.

Animals

Male albino rats (180-200gm body weight) were obtained and purchased from the Pharmacy Department of Jahangir Nagar University, Savar, Bangladesh, and were used for the determination of an abnormal high concentration of glucose in blood. Before using the rats for experiment, they could acclimatize to the laboratory condition for a week at a constant temperature of 22^0C ($\pm5^0$C) with a relative humidity of 40-70% along with the natural 12 hours day-night cycle, in the laboratory of Biotechnology and Genetic Engineering Department, Mawlana Bhashani Science and Technology University, Santosh, Tangail Bangladesh. All described procedures were reviewed and approved by the Mawlana Bhashani Science and Technology University Animals Ethical Committee.

Drugs and chemicals

All drugs and biochemical components used in this experiment were purchased from the different research laboratories in Dhaka region, Bangladesh and the chemicals were of analytical grade.

Preparation of C. tamala leaf solvent extraction

Firstly, 10gm of air dried *C. tamala* leaf powder was placed in a conical flask containing 100 ml (95%) ethanol and was plugged with cotton. Then it was shaken for several times to form a fine mixture of solution. After proper shaking it was filtered through a filter paper and then was centrifuged for 15 minutes. Then Supernatant was collected and evaporated to make final volume which is actually one-fourth of the original volume. Finally the mixture was stored at 4^0C in air tight test tubes.

Experimental design

In the experiment, Animals were divided into four groups consisting of a minimum of three rats each. There were total 12 rats, including 9 diabetic surviving rats and 3 normal rats. Here, Group I was normal rats, Group II was Diabetes induced but non-treated with standard drug and *C. tamala* leaf extracts, Group III received treatment of *C. tamala* leaf extract in different amount of 1.0ml, 1.5ml and 2.0ml with lab diet and the Last group serves as a positive control received the standard drug (glibenclamide) at the dose of 5mg/10ml WFI/kg of body weight. Before starting an experiment, the rats were weighed and carefully marked on the tail, right front, right back, left front, left back, and unmark which was later used as an identification mark for a particular rat before and after the drug administration which could be noted separately.

Preparation of the solutions and reagents

Alloxan

Alloxan monohydrate ($C_4H_2N_2O_4.H_2O$) was available in colored bottles containing 25gm powder. The solution was prepared by dissolving 55 mg in 5 ml of WFI per kg of rat's body weight. The average weight of my grouped rats was 200gm. That's why each rat has been injected 1 ml of prepared Alloxan solution.

Experimental induction of diabetes

Normally, Animals are allowed to fast for 12 hr and when they are administered with freshly prepared Alloxan monohydrate 150mg/kg body weight intravenously but in this experiment, we used 55mg/10ml WFI/kg body weight.[13] This dose permanently destroys the beta cells of pancreas and produces diabetes mellitus. Blood glucose levels of all surviving rats were determined after 4 days of injecting Alloxan monohydrate. Rats with fasting serum glucose level more than 7mmol/L were considered diabetic and were selected for further study.

Dose and route of administration

For the evaluation of hypoglycemic activity, *C. tamala* leaf extracts were provided with lab diet at a dose of daily 1ml for rat-1, 1.5ml for rat-2 and 2.0ml for rat-3 for 18 hours. For all the pharmacological studies the drug glibenclamide was provided as a drug control at a dose of 5mg/10ml/kg body weight.

Measurement of blood glucose concentration

Blood samples were collected on the initial days for 4 weeks by amputation of the tail tip under diethyl ether anesthesia. Just before cutting the tail was immersed into warm water (40^0C) for approximately 22 seconds for

vasodilatation. The level of blood glucose was determined initially and then continuously for 4 weeks. After cutting the tail tip 0.2 ml blood was taken cautiously and the blood glucose level was measured by Glucometer (Glucoleader Enhance, HMD biomedical, Taiwan) using blood glucose test strip (FIA biomed, Germany) as per the supplied manufacturers protocol).

RESULTS

The present study evaluates the anti-hyperglycemic activity of *C. tamala* leaf extract (CTLEt) on blood glucose of Alloxan-induced male albino diabetic rats. Alloxan-induced hyperglycemia has been described as a useful experimental model to study the activity of hypoglycemic agents. Alloxan destroys beta-cells of the pancreas and induces hyperglycemia. In the study, experimental rats were divided into four Groups. Group I - Non diabetic control (only treated with laboratory diet), Group II - Diabetic Control (Alloxan-induced and treated with laboratory diet) and Group III –Diabetic rats administered with *C. tamala* leaf extract (CTLEt) in doses of 1 ml,1.5 ml and 2.0ml and Group IV- Diabetic rats administered with Glibenclamide at a dose of 2.5mg/10ml.

Measurement of the blood glucose levels

Firstly the blood glucose levels of all rats were measured in fasting conditions. In this experiment, blood glucose levels of all Albino rats were measured by Glucometer. The blood glucose levels of Group-I (Normal control) were treated with normal laboratory diet. Blood glucose levels of all rats in Group-I (Normal control) was normal. Group-II (diabetic control) rats were Alloxan induced and treated with normal laboratory diet and blood glucose levels were 7.0mmol/L which meant those rats were in diabetic conditions. All rats of Group-III were treated with different doses of *C. tamala* leaf extracts. The blood glucose levels of all the rats in Group-IV (Medicine + lab diet) according to a disciplined way from fasting conditions then in every two hours of regular intervals up to eighteen hours all the readings were recorded. Fasting blood glucose (FBG) levels of each rat was taken every two hours of interval. More significant ($p<.05$) anti-hyperglycemic activity was observed after eighteen hours of feeding in chronic Alloxan induced type-II diabetic model Albino rats. Table 1 shows group-I (Normal Control) mean blood glucose levels were increased to 18.81% which was considered a normal condition for normal rats and for group-IV (Medicine + lab diet) mean glucose levels decreased to 55.31% which was good. On the other hand for group-III (Diabetic rat + Leaf extract + lab diet) the mean glucose level was decreased to 58.04 % which was higher than medicine and proved that *C. tamala* leaf extract worked against hyperglycemic activity and converted into hypoglycemic condition. These levels of reduction were much higher than medicine treated rats except 1.0ml solution of sample induction. We found 2.0ml solution of sample most effective. Table 2 shows the comparison of four groups in SE value. Values were statistically significant at $p < 0.01$ as compared with diabetic control. Figure 1 shows that after two hours of feeding glucose levels were gradually increased. For group-I (normal control) mean glucose level was normal but due to induction of Alloxan group-II (diabetic control), group-III (CTLEt + lab diet), group-IV (medicine + lab diet) mean glucose levels were higher than group-I (normal control). Fasting blood glucose (FBG) levels of each rat was taken every two hours of interval. More significant ($p<0.05$) anti-hyperglycemic activity was observed after eighteen hours of feeding in chronic Alloxan induced type-II diabetic model Albino rats.

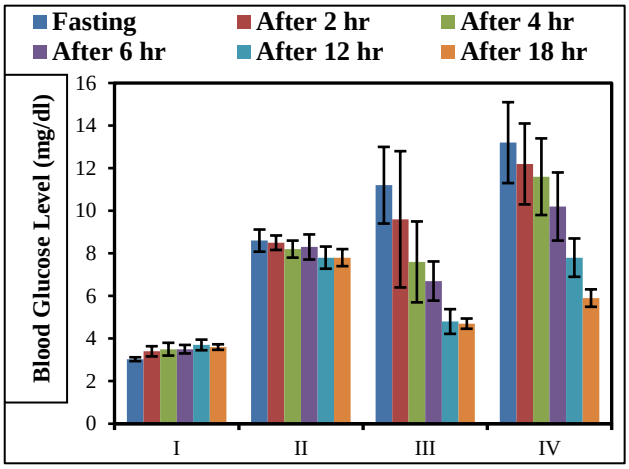

Figure 1: Blood glucose levels in different groups of treated rats.

Table 1: Comparisons among four groups with percentage (mean±percentage).

Groups	Fasting mean glucose level	After 2 hours mean glucose level	After 4 hours mean glucose level	After 6 hours mean glucose level	After 12 hours mean glucose level	After 18 hours mean glucose level
Group-I (Normal Control)	3.03 (100%)	3.4 (112.21%)	3.5 (115.51%)	3.5 (115.51%)	3.7 (122.11%)	3.6 (118.81%)
Group-II (Diabetic Control)	8.6 (100%)	8.5 (98.83%)	8.2 (94.16%)	8.3 (96.51%)	7.8 (90.69%)	7.8 (90.69%)
Group-III (CTLEt treated Control)	11.2 (100%)	9.6 (85.71%)	7.6 (67.85%)	6.7 (59.82%)	4.8 (42.86%)	4.7 (41.96%)
Group-IV (Medicine control)	13.2 (100%)	12.2 (92.42%)	11.6 (87.12%)	10.2 (77.27%)	7.8 (59.09%)	5.9 (44.69%)

Table 2: Comparisons among four groups (mean±SE).

Groups	Fasting mean glucose level	After 2 hours mean glucose level	After 4 hours mean glucose level	After 6 hours mean glucose level	After 12 hours mean glucose level	After 18 hours mean glucose level
Group-I (Normal Control)	3.03±0.09	3.4±0.24	3.5±0.30	3.5±0.21	3.7±0.25	3.6±0.13
Group-II (Diabetic Control)	8.6±0.52	8.5±0.34	8.2±0.41	8.3±0.61	7.8±0.52	7.8±0.40
Group-III (CTLEt treated Control)	11.2±1.8	9.6±3.2	7.6±1.9	6.7±0.92	4.8±0.58	4.7±0.24
Group-IV (Medicine control)	13.2±1.9	12.2±1.9	11.6±1.8	10.2±0.16	7.8±0.91	5.9±0.41

Each value represents mean; ± =SE; CT = *Cinnamomum tamala* leaf extracts, Values were statistically significant at $p < 0.01$ as compared with diabetic control, $p < 0.01$ as compared with normal.

Table 3: Comparison between blood glucose level for the *Cinnamomum tamala* leaf extract treated Group III and Medicine Treated Control Group IV).

No of Sample	Groups	Fasting condition	After 2 h	After 4 h	After 6 h	After 12 h	After 18 h
Rat-1 (1.0ml of CTLEt and lab diet)	G-III	8.6	7.3	5.9	6.8	5.9	5.1
	G-IV	13.9	13.4	12.9	11.5	8.1	6.5
Rat-2 (1.5 ml of CTLEt and lab diet)	G-III	10.4	5.6	5.4	5.1	3.9	4.9
	G-IV	16.3	14.9	13.8	12.1	9.2	6.1
Rat-3 (2.0 ml of CTLEt and lab diet)	G-III	14.7	16.1	11.6	8.3	4.7	4.3
	G-IV	9.3	8.4	8	7.1	6.2	5.1

Table 3 shows that administration of *Cinnamomum tamala* leaf extract (CTLEt) and the Medicine treated on the diabetic induced rats, it was lowered the blood glucose level. Administration of the increasing dosage 1.0ml, 1.5ml and 2.0ml of *Cinnamomum tamala* leaf extracts produced dose-dependent significant reductions in the blood glucose level of alloxan induced rats after 2 hours, 4 hours, 12 hours and 18 hours of treatment.

DISCUSSION

Results of the present study partially support the findings of and significant increase in body weight after treatment with herbal preparations in hyperglycemic animals.[14,15] Similar results were reported after oral administration of the methanol fraction of *Salacia* re*ticulata* twice daily to the diabetic animals which gained body weight.[16] It is now established that there is a gradual decrease in beta-cell function and that may increase the risk of developing type-II diabetes.[17-19] In this study we investigated the use of *Cinnamomum tamala* as antidiabetic agent. Alloxan-induced hyperglycemia has been a useful experimental model to study the activity of hypoglycemic agents.[20]

Alloxan was used to induce diabetes because it is known to cause degranulation to the beta cells of the pancreas. In our study three doses (1.0 ml, 1.5ml, 2.0ml) of the ethanolic extract of *C. tamala* leaf and Glibenclamide drug did not show any significant changes in the fasting blood glucose levels when compared to untreated control after 2 h of treatment. However, after 4, 6, 8, 12 and 18 hours of treatments the extract showed a significant ($P<0.5$) decrease in the fasting blood glucose level when compared to untreated control and 2.0ml dose was found to be more effective in the glycemic change than the 1.0ml and 1.5 ml doses. This shows that the extract does exhibit dose dependent activity.

The extract at a dose of 2.0ml showed a gradual reduction of the fasting blood glucose level 2 h after the administration of the extract.

The result of this present study indicated that *Cinnamomum tamala* leaf extract significantly reduce the blood sugar level in alloxan diabetic rats. The ethanol extract exhibited significant anti-hyperglycemic effect without causing hypoglycemia.

CONCLUSION

In conclusion, it may be stated that our observations are suggestive of the fact that the ethanol extract of C. *tamala* leaves possess antidiabetic activity in normal and diabetic male albino rats and can be improve the oral glucose tolerance (OGT) test by promoting the peripheral utilization of glucose and increasing the muscle glycogen store probably induced by stimulating insulin release from β-cells or through its insulin like action. The results are quite promising and demands further investigation.

ACKNOWLEDGEMENTS

The authors are greatly thankful to the Department of Biotechnology and Genetic Engineering, Mawlana Bhashani Science and Technology University, Tangail, Bangladesh for the logistic supports.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Shibly AZ, Suborna LA, Adhikari J, Islam MS. Evaluation of antihyperglycemic activities of Bangladeshi medicinal plant *Cinnamomum tamala* Leaf extracts in alloxan treated Albino Rats. Int J Basic Clin Pharmacol 2018;7:11-5.