

**Original Article****Effect of aqueous extract of *Carica papaya* leaves on blood glucose level in streptozotocin induced diabetic rats**Syful Islam^{1*}, Jiaul Hasan², Faizul Ahasan³, Eliza Omar Eva⁴¹ Department of Pharmacology, Shaheed. M. MonsurAli Medical College, Sirajganj, Bangladesh.² Department of Pharmacology, Manikganj Medical College, Manikganj, Bangladesh.³ Medical Office Medicine Sanfrontier's Belgium, (kamrangirchor, Dhaka), Bangladesh.⁴ Department of Pharmacology, Dhaka Medical College, Dhaka, Bangladesh.

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E-mail address: syful48dmc@gmail.com; Mobile: +8801757818972**Running Title:** Effect of *Carica papaya* in streptozotocin induced diabetic rats**Received: 07 September, 2016; Revised: 14 October 2016 Accepted: 29 October, 2016**Available online at <http://www.thescientificpub.com><http://dx.doi.org/10.19046/abp.v03i05.03>**Abstract**

The purpose of the study was to investigate the change in blood glucose level following administration of aqueous extract of *C. papaya* leaf in streptozotocin (STZ) induced diabetic rats. The rats were randomly divided into 4 groups having 6 rats in each group. Study was divided into Experiment-1 composed of normal rat groups and Experiment-2 having diabetic rat groups. In Experiment -1 Group A served as control and Group B was given papaya leaf extract 200mg/kg/day orally for 14 days. In Experiment-2 Group C and Group D were given intraperitoneal administration of 65mg/kg of STZ for induction of diabetes. Group D received papaya leaf extract 200mg/kg/day orally for 10 days. Fasting blood glucose level was estimated on day 1, day 4 and day 15. Collected data were tabulated & statistical analysis was done by Student's unpaired t test. P value < 0.05 was considered as statistically significant. Following administration of papaya leaf extract nondiabetic rat group showed no significant change ($p > 0.10$) in blood glucose level but diabetic rat group showed statistically significant differences ($P < 0.001$). This indicates that the extract has blood glucose lowering effect on diabetic rats and so may be effective in managing diabetes mellitus.

Keywords: Aqueous extract, *caricapapaya*, streptozotocin, diabetes mellitus, hypoglycemic effect.**Introduction**

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. It is defined by documenting blood glucose in fasting state (≥ 7.0 mmol/L) or 2 hours after an oral standard glucose drink (≥ 11.1 mmol/L). Acute life-threatening consequences of uncontrolled diabetes are hyperglycemia with ketoacidosis or the nonketotic hyperosmolar syndrome. Long-term complications of DM include retinopathy with potential loss

of vision, nephropathy leading to renal failure; peripheral neuropathy with risk of foot ulcers, amputations, and charcot joints, and autonomic neuropathy causing gastrointestinal, genitourinary, and cardiovascular symptoms and sexual dysfunction [1]. The prevalence of diabetes for all age groups worldwide was estimated to be 2.8% in 2000 and 4.4% in 2030. The number of diabetic population was estimated to rise from 171 million in 2000 to 366 million in 2030. A recent report suggest that highest relative increase will occur in the Middle East, Sub-Saharan Africa and India [2].

Carica papaya is used extensively in traditional societies to treat diabetes [3]. Papaya plantto contain alkaloids, carpain, nicotine, flavinols, tannins, and terpinenes as well as enzymes such as papain and chymopapain [4]. Different parts of *C. papaya* are used in Mexican folk medicine to treat various diseases such as diarrhea, inflammation and diabetes [5].

A few studies in Nigeria, Mexico and Malayasia revealed blood glucose lowering effect following administration of papaya leaf extract in experimental animals. Though the plant is available in almost all districts in our country, study to detect effect of papaya leaf extract on blood glucose level has yet not done in Bangladesh. That is why attempt has been made to evaluate the anti-diabetic effect of *C. papaya* leaves extract on experimental diabetic rats.

Materials and Methods

Ethical consideration

The researcher was duly concerned about the ethical issues related to the study. Formal ethical clearance was taken from the ethical review committee of Dhaka Medical College, Dhaka, Bangladesh for conducting the study. The present study is an experimental one involving animals. Proper permission regarding animal purchase, transport, housing, administering food and extract, and collecting blood glucose sample was obtained from proper authority.

NB: No human subject was included in this study. Only rats were used.

Design, subjects and Statistics

The study was carried out in the Department of Pharmacology, Dhaka Medical College, on 24 albino rats within a duration of 14 days. *C. papaya* leaves were collected from local garden. The plant was authenticated as *C. papaya* (Papaya) leaves by Bangladesh National Herbarium, Mirpur, Dhaka. DACB Accession number 39572. Aqueous extract was made from the Drug Research Laboratory of Center for Advanced Research of Sciences (CARS) of Dhaka University. Total 24 albino rats were purchased from Bangladesh Centre for Scientific and Industrial Research (BCSIR) Lab, Dhaka. They were of either sex, weighing about 140-150 gm. Rats were randomly divided into 4 groups of 6 in each group. In Experiment-1 Group A (control group)- was given standard rat diet for 14 days and Group B was given aqueous extract of *C. papaya* 200mg/kg/day orally along with standard rat food for 14 days. Fasting blood glucose level was estimated on day 1 and day 15 of the experiment. In Experiment 2 Group C and Group D were given intraperitoneal administration of 65mg/kg of streptozotocin

(STZ) for induction of diabetes on day 1. After STZ injection Group C was given standard food for 14 days and Group D- was given standard food for 3 days followed by aqueous extract of *C. papaya* leaves 200mg/kg/day orally along with standard food upto 14th day of the experiment. Fasting blood glucose level was estimated on day 1 (before STZ) on day 4 and on day 15 of the experiment.

Blood sample was collected from each of the animal by aseptically cutting the tail at the tip with a sharp sterile blade under local anesthesia and blood glucose estimation was done by digital electronic glucometer.

Results

Obtained data on fasting blood glucose level from different rat groups were recorded and compiled. Data were expressed as (Mean \pm SD) and tabulated and presented accordingly in tables (1 to 3) and Figures (1 to 3). Statistical analysis was done by appropriate significant test. Unpaired Student's t test was used to compare the results between individual groups of experiments 1 and 2. Test result was considered as statistically significant at P value < 0.05.

Table 1: Showing the effect of aqueous extract of *Carica papaya* leaves on blood glucose level in nondiabetic rats after 2 weeks experiment.

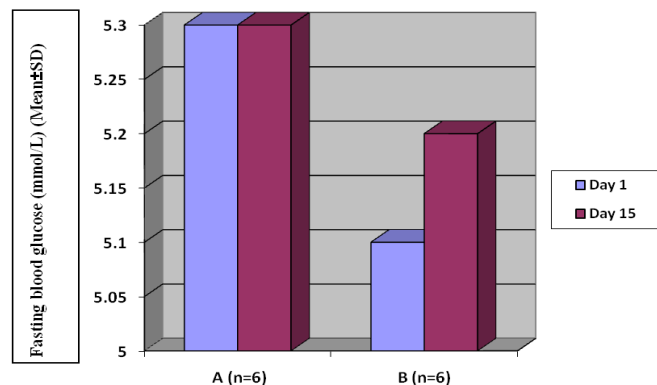
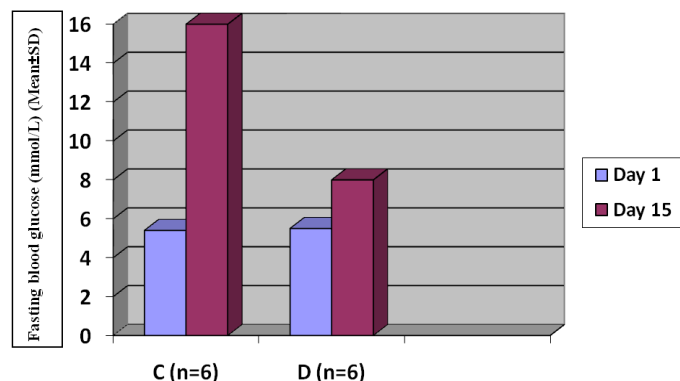
Group	FBG (mmol/L) on day 1 (Mean \pm SD)	FBG (mmol/L) on day 15 (Mean \pm SD)	P value
A (n=6)	5.30 \pm 0.37	5.30 \pm 0.25	>0.10
B (n=6)	5.10 \pm 0.34	5.20 \pm 0.41	

Table 2: Showing the effect of STZ on blood glucose level of group C and group D rats on day 4.

Group	FBG (mmol/L) on day 1 (before STZ) (Mean \pm SD)	FBG (mmol/L) on day 4 (after STZ) (Mean \pm SD)	P value
C (n=6)	5.40 \pm 0.21	15.00 \pm 3.33	>0.10
D (n=6)	5.50 \pm 0.44	15.10 \pm 3.19	

Table 3: Showing the effect of aqueous extract of *Carica papaya* leaves on blood glucose level in diabetic rats.

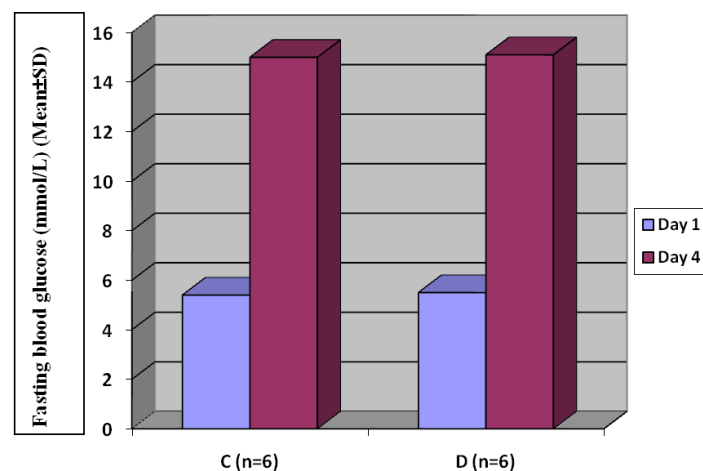
	FBG (mmol/L)	FBG (mmol/L) on	
Group	on day 1	day 15	P value
	(Mean±SD)	(Mean±SD)	
C (n=6)	5.40±0.21	16.00±3.49	<0.001
D (n=6)	5.50±0.44	8.00±1.96	

**Figure 1:** Bar diagram showing fasting blood glucose level (mmol/L) (mean ±SD) in group A and group B rats on day 1 and day 15.**Figure 2:** Bar diagram showing fasting blood glucose level (mmol/L) (mean±SD) in group C, and D rats on day 1 and day 4.

Discussion

The present study was carried out to evaluate the anti diabetic effect of *C. papaya* leaves on experimentally induced diabetic rats. The blood glucose lowering effect of aqueous extract of papaya leaves was tested in non diabetic and experimentally induced diabetic rats. The aqueous extract of papaya leaves was given for 14 day in non-diabetic rats and for 10 days in STZ induced diabetic rats.

Diabetes was induced by STZ. The dose and route of administration of STZ was selected from Omomkhuaet al [3]. The blood glucose levels in animals were measured 72 h after administration of STZ which was done according to experiment of Daye Cheng et al [6] and Akbarzadeh et al [7].

**Figure 3:** Bar diagram showing fasting blood glucose level (mmol/L) (mean±SD) in group C and Drats on day 1 and day 15

In this study, intraperitoneal (i.p) administration of single dose of STZ (65mg/kg), increased blood glucose level significantly. Similar observations were reported by number of researchers. Lal VK et al [8] observed the condition of diabetes after 48 h of intraperitoneal injection of STZ (50 mg/kg) freshly prepared in 0.1M sodium citrate buffer at a dose of 50mg/kg in healthy wistar albino rats. In the present study, the rise of blood glucose level in experimental diabetic rats was also very high. Thus, the findings of this study are in well agreement with the findings of other researchers. The dose of *C. papaya* leaves (200mg/kg body weight), used in this study was selected in keeping conformity with the dose used in research work by Omomkhuaet al [3].

There was no significant change ($P>0.05$) in the mean value of blood glucose level of non diabetic rats treated with aqueous extract of papaya leaves as compared with normal control. It may be concluded that *C. papaya* leaves has no effect on lowering the blood glucose level in nondiabetic rats. Decreased mean value of blood glucose

level was observed in the experimental diabetic group when treated with aqueous extract of *C. papaya* leaves at dose of 200mg/kg body weight changes were significant ($P < 0.001$). Therefore, the findings of this study are in well agreement with the findings of the other researchers Omonkhua et al [3]. It may be concluded that aqueous extract of *carica papaya* leaves has blood glucose lowering effect in experimentally induced diabetic rats.

Juárez-Rojop et al⁵ studied the effect of aqueous extract of *C. papaya* leaves on STZ induced diabetic rats and finding of the study indicated that consumption of the aqueous *C. papaya* leaf extract may act by stimulating the few remaining β -cells with the subsequent release of more insulin, instead of pointing to the regeneration of β -cells of the islets as responsible for the insulin increase.

Sasidharan et al [9] studied antihyperglycaemic effects of ethanol extracts of *C. papaya* leaf in STZ induced diabetic mice at a dose of 100 mg/kg body wt and found statistically significant antihyperglycemic effect. Preliminary phytochemical analysis of *C. papaya* leaves revealed the presence of tannins, flavonoids, saponins, alkaloids, anthraquinones, cardiac glycosides, steroids, reducing sugars, cardenolides and phenolics compounds [10].

C. papaya leaves are believed to exert their anti-diabetic effects by several mechanisms including slowing down digestion inhibiting α -amylase and α -glucosidase and regulating intestinal brush border transport of glucose.³ It has also been demonstrated that hypoglycemic effect of papaya leaf was due to either a decrease in the rate of intestinal glucose absorption or an increase in peripheral glucose utilization. In this line, some authors have ascertained increased catabolism of glucose due to GLUT4 translocation to the plasma membrane in muscle and brown adipose cells. Moreover, a possible stimulatory mechanism on the few surviving β -cells has been considered, which could allow the release of more insulin

and administration of plant extracts can be effective in cell regeneration and restoration of islet size, even producing cell hyperplasia [5].

It was observed that the aqueous extract of *C. papaya* leaves has glucose lowering effect in STZ induced diabetic rats but no effect on blood glucose level on non diabetic rats. The result suggested that the aqueous extract of *C. papaya* leaves may be a useful anti hyperglycemic agent in the treatment of diabetes mellitus. Further investigation may be suggested to measure plasma insulin level, hemoglobin A_{1c}, liver glycogen level, lipid hydro peroxidation level and free radical in the tissues after treatment with aqueous extract of *C. Papaya* leaves.

Conclusion

From our study it is revealed aqueous extract of *C. papaya* leaves may be a useful anti hyperglycemic agent in the treatment of diabetes mellitus.

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Conflict of Interest

Authors declare that there is no conflict of Interest to reveal.

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