

Hypoglycemic Activity of *Carica papaya* Leaf Aqueous Extract in Normal and Diabetic Mice

Renu Kumari Sinha, Raghendra Pratap and Manish Chandra Varma*

University Department of Zoology

TMBU Bhagalpur

Bihar, India

ABSTRACT

The hypoglycemic effect of aqueous extract of *Carica papaya* leaves was investigated on alloxan monohydrate induced diabetic mice. The blood glucose levels were measured at 0, 2, 4 and 6 h after the treatment. The aqueous extract of *C. papaya* (250 mg/kg) reduced the blood glucose of normal mice from 85.50 ± 1.22 to 64.67 ± 3.27 mg/dl, 3 h after oral administration of the extract ($P < 0.05$). It also significantly lowered blood glucose level in alloxan induced diabetic mice from 331.67 ± 4.90 to 130.33 ± 6.53 mg/dl, 6h after oral administration of the extract ($P < 0.05$).

Keywords: *Carica papaya*, Antihyperglycemic, Hypoglycemic, Alloxan monohydrate, aqueous extract.

1. INTRODUCTION

Diabetes mellitus is a assemblage of metabolic disorders characterized by hyperglycemia and 1.3 % of the population suffers from this disease throughout the world (ADA, 2017). These metabolic disorders include alteration in the carbohydrate, fat and protein metabolism associated with absolute or relative deficiencies in insulin secretions and/or insulin action. The distinguishing symptoms of diabetes are polyuria, polydipsia, polyphagia, and unexpected weight loss. (Altan,2003).

Besides hyperglycemia, several other factors including dislipidemia or hyperlipidemia are involved in the development of micro and macrovascular complications of diabetes, which are the major causes of morbidity and death (ADA, 2014). Many herbal products have been described for the cure for diabetes mellitus in ancient literature. There is an increasing demand by patients to use the natural products with antidiabetic activity due to side effects associated with the use of insulin and oral hypoglycemic agent such as sulfonylureas, metformin, α -Glucosidase inhibitors, Troglitazone, (Holman and Turner,1991).

The available literature shows that there are more than 400 plant species showing hypoglycemic activity (Kameswara Rao et al., 1997) and presently several laboratories are involved in isolating new herbal hypoglycemic agents. Though some of the plants are reputed in the indigenous system of medicine for their activities, it remains to be scientifically established. *C. papaya* a medium tree belonging to the family of Caricaceae, reaching 2-3 m in height, frequently met with in peninsular India in the eastern and Western ghats upto 1,200 m, in the coastal plains, and in the hills of North-eastern India (Gupta, 1994). The root is used as antipyretic, tonic to the liver, diseases of the blood, leucoderma, bronchitis, and asthma (Deysi,2014) . The present study focused to evaluate aqueous extract of *C. papaya* in normal and alloxan-induced diabetic mice.

2. EXPERIMENTAL DETAILS

2.1 Plant material

The leaves of the plant were collected from the leaves of *C. papaya* were collected from botanical garden of T.M Bhagalpur university, Bhagalpur District in the month of November-2017 and cleaned to remove the debris. The collected plant was identified and authenticated by a botanist Dr. A.K Roy, Department of Botany, T.M Bhagalpur university, Bhagalpur. The leaves were dried at room temperature for 10 d and coarsely powdered with the help of a hand grinding mill and the powder was passed through sieve No. 60.

2.2 Preparation of the extract

The powder of leaves of *C. papaya* was extracted separately by continuous hot extraction process using soxhlet apparatus. After extraction, the extracts were concentrated under reduced pressure in tared vessel. The dry extracts were subjected to various chemical tests to detect the presence of different phyto constituents.

2.3 Animals

Male Albino mice of approximately the same age, weighing about 25-30 g, bred in the Animal House, University of Zoology, Sciences campus, T.M Bhagalpur University, Bhagalpur were used in this study.

They were housed in polypropylene cages and fed with standard chow diet and water *ad libitum*. The animals were exposed to alternate cycle of 12 h of darkness and light each. Before each test, the animals were fasted for atleast 12 h. The experimental protocols were subjected to the scrutinization of the Institutional Animal Ethics Committee and were cleared by the same.

2.4 Acute toxicity studies

Swiss albino mice of either sex and of approximately the same age, weighing about 20-30 g were used for the acute toxicity studies. The animals were divided into control and test groups containing six animals each. The control group received the vehicle (1 % acacia gum) while the test groups got graded doses of different extracts orally and were observed for mortality till 48 h and the LD50 was calculated.

2.5 Induction of diabetes

Animals were fasted for 24 hours and injected with freshly prepared aqueous solution of alloxan monohydrate (150 mg/kg i.p.) as reported previously (Dunn and Mclethie, 1943). After a week, mice with marked hyperglycemia (fasting blood glucose >300 mg/dl) were employed for the study.

2.6 Effect of *C. papaya* on blood glucose level in mice

Different groups of mice were used to study the effect of aqueous extract of *C. papaya*. The animals were divided into four groups each consisting of 6 mice. First and second groups were served as untreated, normal control and diabetic control and fed on distilled water alone. Third and fourth groups were normal mice and diabetic mice respectively, treated with aqueous extract (250 mg/kg) of leaves of *C. papaya*. After an overnight fast, the plant extract suspended in 5 % gum acacia was fed by gastric gavage. Blood samples were collected for the measurement of blood glucose from the tail vein at 0, 2, 4 and 6 hours (Davis and Granner, 1996) after feeding the plant extracts. The blood glucose level was determined by the O toluidine method of Fings et al (1970).

Plasma insulin was assayed by the modified method of Herbert et al (1965) using insulin radioimmunoassay kit obtained from BARC, Mumbai, India. Dextran coated charcoal in 0.2 M glycine buffer was used to separate bound and free insulin. Standard curve range was 3.9–250 μ U/ml insulin.

3. STATISTICAL ANALYSIS

All values were expressed as mean \pm SEM. The data were statistically analyzed using one way ANOVA followed by Newman Keul's multiple range test and differences below $P < 0.05$ are considered as significant.

4. RESULTS AND DISCUSSION

The leaves of *C. papaya* were collected from botanical garden of T.M Bhagalpur university, Bhagalpur and extracted. The average percentage yield of alcohol extract of *C. papaya* was found to be 2.6 % w/w. The preliminary phytochemical screenings of the aqueous extract of leaves of *C. papaya* revealed the presence of alkaloids, glycosides, saponins, phytosterols, tannins and amino acids. The LD50 of the aqueous extract was found to be 2495 mg/kg.

The effect of aqueous extract of *C. papaya* on fasting blood glucose level was assessed in normal and diabetic mice at various time intervals are shown in Table-1. The mean blood glucose level was decreased from 85.50 ± 1.22 to 64.67 ± 3.27 mg/dl in normal mice treated with aqueous extract of *C. papaya* ($P < 0.05$). A significant decrease in blood glucose level was observed in the diabetic group treated with *C. papaya* from an initial level of 331.67 ± 4.90 to 130.33 ± 6.53 mg/dl, 3 hours after administration extract.

The effect of aqueous extract of *C. papaya* on plasma insulin levels in normal and diabetic mice is shown in Table- 2. The plasma insulin levels in diabetic group were decreased significantly compared to that of normal groups. In the diabetic mice with the treatment of aqueous extract of *C. papaya*, the insulin levels were significantly increased to 18.33 ± 0.82 μ U/ml from an initial value of 8.67 ± 0.49 μ U/ml. In the normal treated mice also there was a slight increase in insulin levels after the treatment with aqueous extract of *C. papaya*. In this study the aqueous extract of *C. papaya* at the dose of 250 mg/kg produced a significant fall in the blood glucose level in both normal and diabetic mice and this was evident 2 hours after the administration of the extracts.

The antihyperglycemic activity of aqueous extract of *C. papaya* was associated with an increase in plasma insulin levels, suggesting that the activity could be due to insulinogenic activity of the extract. The increased levels of insulin in diabetic treated mice in this study, indicate that the aqueous extract of *C. papaya* stimulates insulin secretion from the remanent β cells or/and from regenerated β cells. Similar effect, i.e. insulinogenic activity with the treatment of some medicinal plants was shown by Karunanayake et al. (22) and Cakici et al. (23). Further investigation is expected to characterize the active hypoglycemic principle. In present studies the aqueous extract of *C. papaya* produced the maximum glucose lowering activity in chemically induced diabetic mice after 3 hours and produced significant hypoglycemic activity in normal

Table1. Effect of aqueous extract of *C. papaya* on fasting blood glucose levels in normal and diabetic mice

Groups	Dose (mg/kg)	Fasting blood glucose at different hours after the treatment (mg/dl)			
		0h	2h	4h	6h
Untreated normal	-	84.17 \pm 1.19	85.33 \pm 1.31	85.17 \pm 1.55	86.17 \pm 1.88
Treated normal	250	85.50 \pm 1.22*	72.67 \pm 1.63	70.50 \pm 2.37*	64.67 \pm 3.27
Untreated diabetics	-	332.50 \pm 7.11	334.33 \pm 6.53	338.67 \pm 5.22	340.50 \pm 3.51
Treated diabetics	250	331.67 \pm 4.90	224.33 \pm 5.72*	195.50 \pm 7.1*	130.33 \pm 6.53*

Values are expressed as Mean \pm SEM, n=6, * $P < 0.05$ when compared with control.

Table 2 Effect of aqueous extract of *C. papaya* on plasma insulin in normal and diabetic mice.

Groups	Dose (mg/kg)	Plasma insulin (μ U/ml)	
		Before treatment	After treatment (6h)
Untreated normal	-	24.33 \pm 0.82	23.67 \pm 1.96
Treated normal	250	8.83 \pm 0.90	7.67 \pm 1.14
Untreated diabetics	--	22.0 \pm 1.31	28.67 \pm 1.63*
Treated diabetics	250	8.67 \pm 0.49	18.33 \pm 0.82

Values are expressed as Mean \pm SEM, n=6, * P<0.05 when compared with control.

5. CONCLUSION

The aqueous extract of *C. papaya* (250 mg/kg) reduced the blood glucose of normal mice from 85.50 \pm 1.22 to 64.67 \pm 3.27 mg/dl, 3 h after oral administration of the extract (P<0.05). It also significantly lowered blood glucose level in alloxan induced diabetic mice from 331.67 \pm 4.90 to 130.33 \pm 6.53 mg/dl, 6h after oral administration of the extract (P<0.05).

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