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# ANTIDIABETIC ACTIVITY AND CHEMICAL CHARACTERIZATION OF AQUEOUS ROOT EXTRACT OF *CARICA PAPAYA* IN ALLOXAN INDUCED DIABETIC RATS

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**ABSTACT**
Diabetes mellitus is a growing health problem in most countries and its incidence is considered to be high all over the world. So, the purpose of this study was to evaluate antidiabetic and chemical characterization of aqueous roots extracts of *Carica papaya* in alloxan induced diabetic rats. Diabetes was confirmed after 5 days of single intraperitoneal injection of alloxan (120 mg/kg) in albino wistar rats. In this study we have taken an aqueous root extracts of *Carica papaya* (100 and 200 mg/kg) and glibenclamide (10 mg/kg, p.o.) orally administered daily for 15 days, blood was withdrawn for glucose determination on 0, 1, 10 and 15 days respectively. At doses of 100 and 200 mg/kg showed significant in blood glucose when compared to diabetic control group. We concluded that aqueous extracts of roots of *Carica papaya* possess Antidiabetic activity..

**KEYWORDS:** Carica papaya, Antidiabetic Activity, Alloxan, Glibenclamide, Aqueous extract.

## INTRODUCTION

Diabetes mellitus is represented by hyperglycaemia, lipidaemia, and oxidative stress; it predisposes affected individuals to long term complications affecting the eyes, skin, kidneys, nerves, and blood vessels.[1-4] Type 2 diabetes mellitus affected individuals more prone with cardiovascular diseases risk rather than individuals not affected with type 2 diabetes mellitus. Diabetes also causes risk of blood pressure and LDL- cholesterol level. Globally diabetes has spread more frequently due to modern lifestyle and it also can be linked to an obesity and sedentary population.[5-7] Alloxan (2, 4, 5, 6-pyrimidinetetrone) is an oxygenated pyrimidine derivative and toxic glucose analogue. It is present as alloxan hydrate in aqueous solution.[8-10]

*Carica papaya*, an herbaceous plant, member of the small family Caricaceae. This plant is widely cultivated for its edible pleasant fruit, which provides good nutritional value and easy digestion. Infusions made from different parts of the plant including roots have been used as therapeutic remedies due to their medicinal properties.[11] There is evidence that *C. Papaya* roots reduce symptoms of asthma, worming and dysentery. Moreover, *C. papaya* root extracts have long been used as remedy for cancer and infectious diseases.[12-13] The root aqueous extract accelerates wound healing.[14-15] On the basis of literature review and tribal information gathered from Kerakat, Jaunpur, Uttar Pradesh that the plant *Carica papaya* (Papita) have reported the use of the roots for the management of diabetes mellitus. However, there is no scientific evidence to support this claim. Hence, the objective of this study was to ascertain the scientific basis for the use of *Carica papaya*. (Caricaceae) in the management of diabetes using alloxan induced diabetic rats.

## MATERIALS AND METHODS

### Chemicals

Alloxan monohydrate was purchased from Sigma-Aldrich Pvt. Ltd (New Delhi, India). Glibenclamide was purchase from local market of Allahabad. All chemicals used including the solvents, were of analytical grade.

### Collection of plant material

The roots of *Carica papaya* were collected from the local area of Allahabad, Uttar Pradesh, India in the month of May to June 2016. Authenticated and specimen was deposited in the herbarium of botanical survey of India, Allahabad utter Pradesh. Ref. No.-98641.

### Preparation of extracts

The *Carica papaya* roots was dried under shade, powdered with a mechanical grinder and passed through a 40-mesh sieve. The successive solvent cold extraction method used to obtain various extracts including petroleum ether, chloroform, ethyl acetate, ethanol and aqueous extracts. The solvents were removed from the extracts under reduced pressure by using a rotary vacuum evaporator. The percentage yield of extracts was calculated and stored in air and water proof containers. The brown extract was obtained and solubility studies

was carried out and used respective solvents for phytochemical screening and pharmacological studies.

**Phytochemical screening**[16]

The *Carica papaya* root extract obtained was subjected to various qualitative tests for identification of the constituents present, by using simple and standard qualitative methods.

**Animals**

Healthy, adult Albino Wistar rats (150-200gm) of either sex were purchased from the central drug research institute of Lucknow used for study. Housed individually in polypropylene cages, maintained under standard conditions (12:12h) light: dark cycle; 25 ± 2°C, 35%–60% humidity). They were fed with standard rat pellet diet (Hindustan Lever Ltd; Mumbai, India). The Institutional Animal Ethics Committee (SIP-IAEC/002/09/16) approved the study.

**Acute toxicity study**[17]

The acute oral toxicity study has to be carried out as per the guidelines set by OECD, revised draft guidelines 423, received from CPCSEA, ministry of social justice and empowerment, Govt. of India.

The animals are randomly selected, marked to permit individual identification, and kept in their cages for at least 5 days prior to dosing to allow for acclimatization to the laboratory conditions. The test substance was administered in a single dose using a stomach tube or a suitable intubation cannula. In the unusual circumstance that a single dose is not possible, the dose may be given in smaller fractions over a period not exceeding 24 hours.

Three animals were used for each step. The dose level to be used as the starting dose is selected from one of four fixed levels, 5, 50, 300 and 2000 mg/kg body weight. The starting dose level should be that which is most likely to produce mortality in some of the dosed animals.

**Induction of diabetes**

The animals were fasted for 12 h prior to the induction of diabetes. A single dose (120 mg/kg, i.p.) of alloxan monohydrate dissolved in 0.5% Tween 80 was used for induction of diabetes in rats after overnight fasting. After 1 h of alloxan administration, the animals were fed standard pellets and water ad libitum. The animals were stabilized for 5 days and animals showing blood glucose level more than 200 mg/dL were selected for the study [18].

**Experimental design**

The rats were randomly divided into five groups comprising of six animals in each groups as given below. Aqueous extracts (100 and 200 mg/kg)/ Glibenclamide (GLB) was administered orally using an oral cannula once daily for 15 days.

**Group I:** normal untreated rats were given 0.5%Tween 80 for 15 days.
**Group II**: Diabetic controls have been given 0.5%Tween 80 for 15 days, 5 days after alloxan (120mg/kg, i.p.) treatment.
**Group III:** Rats have been given aqueous extract of *Carica papaya* (100mg/kg/day, p.o.) for 15 days, 5 days after alloxan (120mg/kg, i.p.) treatment.
**Group IV**: Test rats have been given aqueous extract of (200mg/kg, p.o.) for 15 days, 5 days after alloxan (120mg/kg, i.p.) treatment.
**Group V**: Rats have been given Glibenclamide (10mg/kg/day, p.o.) for 15 days, 5 days after alloxan (120mg/kg, i.p.) treatment.

Blood samples were collected from tail vein of each rat after 0, 1, 2 and 3 and serum glucose was estimated by electronic glucometer. Percent reduction in serum glucose was calculated with respect to the initial level. Five days before the termination of the experiment, the oral glucose tolerance test (OGTT) was performed to assess the glucose tolerance. For this purpose, overnight fasted rats were fed glucose (2 g/kg) orally and blood was collected at 0, 30, 60 and 120 min interval from orbital sinus for glucose estimation.

**Statistical analysis**

**For oral glucose tolerance test**

The data was represented as mean ± SEM. Results was analysed by one way ANOVA followed by Dunnett's multiple comparison tests using Graph pad in stat 3.0 software.

**For anti-diabetic activity**

The data was represented as mean ± SEM. Results was analyzed by one way ANOVA followed by Dunnett's multiple comparison tests. Results were expressed as the mean ± S.E.M. for statistical analysis of the data group means, were compared by one-way analysis of variance (ANOVA) followed by Dunnett's multiple comparison tests. $p < 0.01$ was considered to be statistically significant.

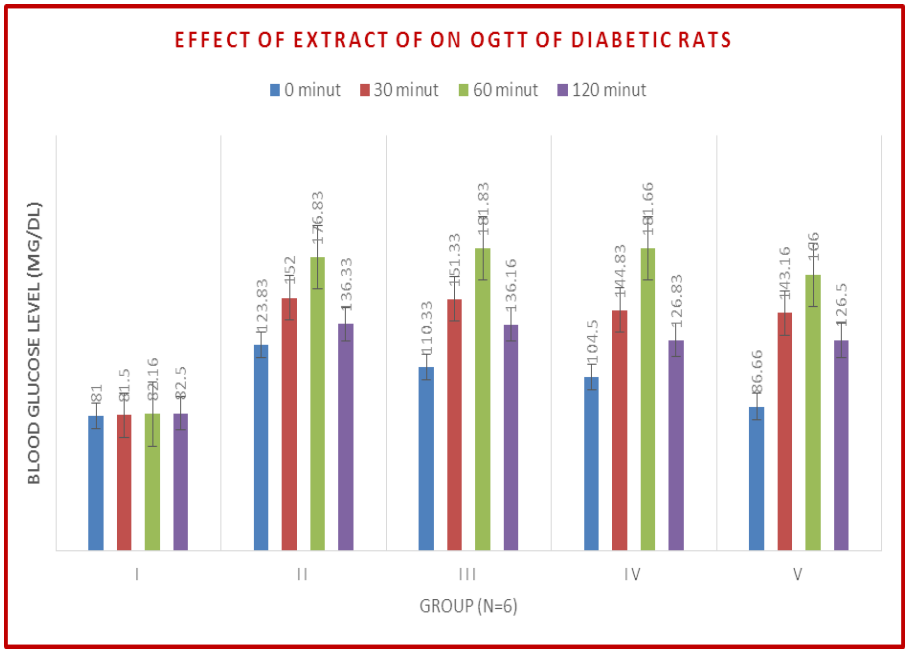
**RESULTS**

Preliminary study was performed on the aqueous extracts of the roots of *Carica papaya* and the presence of various phytoconstituents such as carbohydrates, proteins, amino acids, Saponin, phenolic compounds, alkaloids and flavonoids, glycosides, steroids, fixed oils, and tannins were present. Oral glucose tolerance test (OGTT) in diabetic rats, reported in Table 1 and Fig. 1.

**Table: 1 Effect of aqueous roots extract of *Carica papaya* on OGTT of diabetic rats**

| Groups | Treatment / mg/kg | Blood glucose levels (mg/dl) | | | |
|---|---|---|---|---|---|
| | | 0 min | 30 min | 60 min | 120 min |
| 1 | Normal control | 81 ± 0.73 | 81.5 ± 0.76 | 82.16 ± 0.79 | 82.5 ± 0.76 |
| I | Diabetic control | 123.83 ± 0.79 | 152 ± 0.57 | 176.83 ± 0.70 | 136.33 ± 0.76 |
| III | Aqueous extract (100 mg/kg) | 110.33 ± 0.66 | 151.33 ± 0.49 | 181.83 ± 0.47 | 136.16 ± 0.60 |
| IV | Aqueous extract (200 mg/kg) | 104.5 ± 0.42 | 144.83 ± 0.47 | 181.66 ± 0.33 | 126.83 ± 0.47 |
| V | Glibenclamide (10 mg/kg) | 86.66 ± 0.55 | 143.16 ± 0.60 | 166 ± 0.51 | 126.5 ± 0.56 |

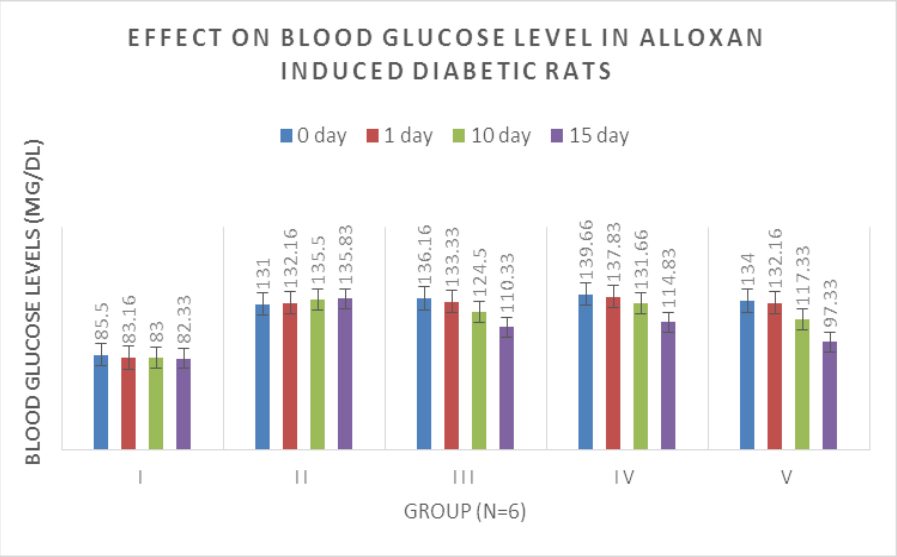
Values are expressed as mean ± SEM for (n=6) rats in each group, when compared to control **p<0.01, *p<0.05 and ns p>0.05.




The effect of treatment of the extracts shows significant reduction on blood glucose levels of diabetic rats, on first day it was found to be 136.16 ± 1.04 of 100 mg/kg treated and 137.83 ± 1.81 of 200 mg/kg and on 15th day it was found to be 110.33 ± 4.67 of 100 mg/kg and 114.83 ± 4.67 of 200 mg/kg, whereas the standard drug Glibenclamide shows the anti-diabetic effect as on 1st day and on 15th day was found to be 132.16 ± 0.60 and 97.33 ± 1.74 respectively, reported in table 2 and Fig 2.

**Table: 2 Effect of aqueous root extracts of Carica *papaya* on blood glucose level in alloxan induced diabetic rats Values are expressed as mean ± SEM for (n=6) rats in each group, when compared to control **p<0.01 and ns p>0.05.**

| Groups | Treatment / Dose | Blood glucose level (mg/dl) | | | |
|---|---|---|---|---|---|
| | | 0 day | 1day | 10 day | 15 day |
| I | Normal control | 85.5 ± 1.54 | 83.16 ± 1.32 | 83 ± 1.54 | 82.33 ± 1.38 |
| II | Diabetic control | 131 ± 1.15 | 132.16 ± 0.87 | 135.5 ± 1.11 | 135.83 ± 1.24 |
| III | Aqueous extract (100 mg/kg ) | 136.16 ± 1.04 | 133.33 ± 0.95 | 124.5 ± 1.66 | 110.33 ± 4.6 |
| IV | Aqueous extract (200 mg/kg) | 139.66 ± 1.60 | 137.83 ± 1.81 | 131.66 ± 1.81 | 114.83 ± 4.67 |
| V | Glibenclamide (10 mg/kg) | 134 ± 0.36 | 132.16 ± 0.60 | 117.33 ± 2.78 | 97.33 ± 1.74 |




## DISCUSSION

The results show that the intraperitoneal administration of Alloxan to rats significantly increased glucose blood levels in five days after injection, as well as decreased body weight. In addition, other diabetes-related signs were observed. These results agree with previous observations that have employed this model and that also report loss of body weight.[19-20] The aqueous extract maintained the body weight of diabetic rats during treatment. Weight loss is a main sign of diabetes but its mechanism is not clear. It could be due to many factors such as loss of appetite, increased muscle waste and loss of tissue proteins. In addition, the administration of the aqueous extract of *C. papaya* decreased water consumption.[21-23] Alloxan induces diabetes by destroying the insulin-producing beta cells of the pancreas. The use of lower dose alloxan (120 mg/kg b.w.) produced partial destruction of pancreatic beta cells even though the animals became permanently diabetic. Thus these animals have surviving beta cells and regeneration is possible.[24-27] Glibenclamide, antihyperglycemic effect by stimulating insulin release from pancreatic beta cells, reducing the hepatic clearance and suppressing the secretion of glucagon.[28] The active constituents responsible for antidiabetic activities are not known. Phytochemical analysis showed the presence of alkaloids, tannins, Saponin, flavonoids, Anthraquninone, anthocyanosides, and reducing sugars.

## CONCLUSIONS

This preliminary study confirms the antidiabetic activity of *C. Papaya* roots in diabetic rats. These results suggest that the aqueous extract of *C. papaya* may improve the metabolic disruption produced by diabetes. However, further research is needed to gain a better understanding of its potential therapeutic action, the implicated phytochemical constituents and the exact mechanism of action.

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