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Research Article

EVALUATION OF ANTI DIABETIC ACTIVITY OF *CARICA PAPAYA* SEEDS ON STREPTOZOTOCIN- INDUCED TYPE-II DIABETIC RATS

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ABSTRACT

A crude extract of *Carica papaya* seeds was prepared in boiling water and the aqueous extract was dried. At a dose of 100 mg/kg, 200mg/kg the extract was given to Male Sprague- Dawley rats for 14 days to evaluate the anti hyperglycemic and anti hyperlipidaemic activity in Streptozotocin - Nicotinamide induced diabetic rats. Glibenclamide was used as a standard drug. The blood glucose levels were determined at different times by glucose oxidase method. Serum Glutamate Oxaloacetate Transaminase (SGOT), Serum Glutamate Pyruvate Transaminase (SGPT) levels and lipid profile was also determined. Dosage of 100mg/kg and 200mg/kg of the extract significantly ($P<0.001$, $P< 0.01$) decreased blood glucose levels and the decrease was found to be dose dependent. SGOT, SGPT levels were decreased ($P<0.01$, $P<0.05$). Lipid profile was also decreased significantly ($P<0.01$, $P<0.05$). In the present study the anti hyperglycemic potential of *Carica papaya* was demonstrated in rats. It also has beneficial effects in diabetes associated complications.

Keywords: Anti-diabetic, *Carica papaya*, Glibenclamide, Nicotinamide, Streptozotocin.

1. INTRODUCTION

Diabetes Mellitus is the common endocrine disease and affects nearly 10% of world population [1]. At present, 347 million people worldwide have diabetes [2]. In 2004, an estimated 3.4 million people died from consequences of fasting high blood sugar [3]. A similar number of deaths have been estimated for 2010. More than 80% of diabetes deaths occur in low- and middle-income countries [4]. For a long time, diabetes has been treated with the medicinal plants based on traditional medicine information. Several plant species have proven to have hypoglycemic effect [5]. Despite of the presence of several antidiabetic agents in the market due to their disadvantages, the search for more effective and safer agents has continued to be an important area of research.

Carica papaya is a medicinal plant. The fruits are used as fodder. Fruit, leaves, latex and stem are used to treat indigestion, diarrhoea, swelling of the lungs, stoppage of urination, blindness, tachycardia, ringworm and alopecia. The seeds are used as anthelmintics. The fruit contains high levels of Vitamins A and C and a phytochemical called β Cryptoxanthin that promotes health. Seeds extract have been reported of having bactericidal activity [6]. The pulverized seeds are documented for antiparasitic activity and for antifertility activity [7].

The seed is a rich source of proteins (27.8% undefatted, 44.4% defatted), lipids (28.3% undefatted) and crude fiber (22.6% undefatted, 31.8% defatted). Of the toxicants estimated, glucosinolates occurs in the highest proportion. The seed is low in free mono saccharides. Sucrose is the predominant sugar (75.0% of total sugars). Mineral content is generally low. However, Calcium and Phosphorus occur in appreciable quantities (17 and 340 µg/g respectively) [8].

2. MATERIAL AND METHOD

2.1. Plant materials

Fruits of *Carica papaya* were collected from the local market of Khammam. They are cut into pieces and seeds were separated thoroughly washed. They are dried at room temperature. The botanical identity of the seeds was authenticated by the taxonomist Dr. V. S. Raju (Kakatiya University, Warangal).

2.2. Extraction

Dried seeds were crushed and grinded in a domestic mixer grinder and coarse powder was prepared. Extract of the dried seed powder was prepared in boiling water. The extract was filtered with a Whatman's filter paper and dried at 40°C. The obtained powder was in chocolate colour with aromatic odor [9]. (Table-1).

2.3. Animals

Male Sprague- Dawley rats with a weight between 180 to 200g obtained from the Mahaveer industries, Hyderabad after approval of the protocol by Institutional Animal Ethics committee (IAEC). Rats were maintained under standard conditions of temperature 22°C, light/dark cycle of 12hrs and food and water *ad libitum*.

2.4. Chemicals

Streptozotocin, Nicotinamide and Glibenclamide were obtained from Sigma laboratories (Germany). Streptozotocin was dissolved in citrate buffer for intraperitonial injection. Nicotinamide was dissolved citrate buffer for intraperitonial administration and Glibenclamide was dissolved in distilled water for oral administration.

2.5. Evaluation of anti-hyperglycemic activity of *Carica papaya* seed extract

2.5.1. Induction of Diabetes and animal treatment

Diabetes was induced in overnight fasted rats by single intraperitonial injection of 65mg/kg of Streptozotocin is dissolved in citrate buffer (pH 4.5), 15 min after the i.p administration of 110mg/kg of Nicotinamide dissolved in normal saline solution. Hyperglycemia was confirmed by the elevated glucose levels in plasma, determined seven days after diabetic induction. Animals with blood glucose concentration more than 150mg/dl were used for study [10].

2.5.2. The animals were randomly divided into five groups and treated as follows

Thirty rats were divided into five groups, each consisting of six animals. The extract was dissolved in water and administered orally. Saline solution and Glibenclamide at 10mg/kg were administered orally as negative and positive controls respectively. Rats were divided into fallowing groups.

Group 1 - Normal untreated rats.

Group 2 - Diabetic untreated rats.

Group 3 - Diabetic rats treated with10mg/kg body weight of Glibenclamide.

Group 4 - Diabetic rats treated with 100mg/Kg body weight of *Carica papaya* seeds aqueous extract for 14 days.

Group 5 - Diabetic rats treated with 250mg/Kg body weight of *Carica papaya* seeds aqueous extract for 14 days.

The animals were fasted overnight for 16hrs with free access to water throughout the duration of the experiment and the blood samples were drawn from the retro-orbital plexus under mild ether anesthesia at 0, 1, 2, 4, 6 and 8 hrs after respective treatments.

3. RESULTS

3.1. Effect of *Carica papaya* seed extract on body weight of Streptozotocin - Nicotinamide induced diabetic rats.

Streptozotocin produces significant loss in body weight as compared to normal animals during the study. Diabetic control continued to lose weight till the end of the study while Carica seed extract at two doses showed significant improvement in body weight compared to diabetic control. Moreover the weight gain was lesser in the diabetic rats when compared to normal control rats. Thus the body weight loss in diabetic rats was only significantly attenuated by plant extract (Table-1).

Table 1: Effect of Carica papaya seed extract on body weight (mean±SD) (n=6) of Streptozotocin - Nicotinamide induced diabetic rats

Groups	Initial weight(g)	Final weight(g)
Normal control	178±8.91	205±9.87
Diabetic control	182±8.40	158±8.50
Diabetic+Glibenclamide (10mg/kg)	194 ±9.24	198±8.23***
Diabetic+ CSET(100mg/kg)	189±8.78	193±10.37***
Diabetic+ CSET(200mg/kg)	190±7.42	209±10.19***

***P<0.001.*P<0.01 compared with diabetic control group. (ANOVA followed by Dunett's test).*

3.2. Effect of *Carica papaya* seed extract on blood glucose levels in Streptozotocin - Nicotinamide induced diabetic rats.

Carica papaya Seed Extract administered at two different doses of 100mg/kg, 200mg/kg to Streptozotocin - Nicotinamide treated diabetic rats caused significant ($P < 0.001$, $P<0.01$) reduction of blood glucose levels which was related to dose and duration of treatment. Maximum reduction was observed on day 14 (Table-2).

3.3. Effect of *Carica papaya* seed extract on liver Transaminase level of Streptozotocin - Nicotinamide induced diabetic rats.

Streptozotocin administration increased liver function biomarkers such as Serum Glutamate Oxaloacetate Transaminase (SGOT), Serum Glutamate Pyruvate Transaminase (SGPT) in comparison to diabetic control rats ($P<0.01$, $P< 0.05$). Transaminases are active in the absence of insulin due to the availability of amino acids in the blood of Diabetes Mellitus. The increase may be due to the leaking out from the tissue and then migrating into the blood stream. In Carica seed extract and Glibenclamide treated groups the cell damage might be reverted and which may lead to decreased activity of SGOT, SGPT (Table-3).

3.4. Effect of *Carica papaya* seed extract on lipid profile Streptozotocin - Nicotinamide induced diabetic rats.

The abnormal high concentration of serum lipids mainly due to the increase in the mobilization of frees fatty acids from the peripheral fat deposits, because insulin inhibits hormone sensitive lipase production. However, administering Carica seed extract to diabetic rats brought the values near to normal level. Thus Carica seed extract exhibited hypocholesterolaemic, hypotriglyceridaemic effects (Table-4).

Table 2: Effect of Carica papaya seed extract on blood glucose levels (mg/dl) (mean±SD) (n=6) in Streptozotocin - Nicotinamide induced diabetic rats

Groups	Blood glucose levels(mg/dl)		
	day1	day7	day14
Control	74.10 ±2.55	76.55±1.76	75.86±2.34
Diabetic control	187.00±3.72	217.24±5.23	232.31±4.27
Glibenclamide (10mg/kg)	178.50±8.78*	132.20±4.14**	92.06±5.29**
CSET(100mg)	184.90±5.24	163.40±8.43*	135.19±6.54*
CSET(200mg)	182.50±6.56	160.10±8.43*	128.00±7.34**

***P<0.001.*P<0.01 compared with diabetic control group. (ANOVA followed by Dunett's test).*

Table 3: Effect of Carica papaya seed extract on liver Transaminase level (IU/ml) (mean±SD) (n=6) of Streptozotocin - Nicotinamide induced diabetic rats

Groups	SGOT(IU/ml)	SGPT(IU/ml)
Control	48.0±2.45	46.5±1.65
Diabetic control	70.0±4.83	88.5±2.38
Glibenclamide (10mg/kg)	57.0±3.56**	51.0±4.45**
CSET (100mg/kg)	62.0±6.72*	60.0±5.22*
CSET (200mg/kg)	54.0±8.27*	58.5±8.27*

***P<0.01, *P<0.05 compared with diabetic control group (ANOVA followed by Dunett's test).*

Table 4: Effect of Carica papaya seed extract on lipid profile (mg/dl) (mean±SD) (n=6) Streptozotocin - Nicotinamide induced diabetic rats

Groups	Triglycerides (mg/dl)	Total cholesterol (mg/dl)
Control	65.0±2.71	77.18±2.24
Diabetic control	86.5±3.53	147.00±5.53
Glibenclamide (10mg/kg)	70.7±5.06**	100.50±8.12**
CSET (100mg/kg)	77.0±4.22*	136.00±6.82*
CSET (200mg/kg)	71.5±7.27**	103.00±7.27**

***P<0.01, *P<0.05 compared with diabetic control group (ANOVA followed by Dunett's test).*

4. DISCUSSION

These studies showed the antihyperglycemic along with hypolipidemic effect of Carica seed extract in Streptozotocin - Nicotinamide induced diabetic rats. The diabetic rats when treated with the Carica seed extract in the dose of 100 and 200mg/kg body weight, showed decline in blood glucose level on 7 and 14th day respectively in dose dependent manner. The abnormal high concentrations of serum lipid levels are also decline to normal levels. Streptozotocin induces diabetes by free radical generation. This causes a massive reduction of insulin secreting beta cells of the islets of langerhans, which results in a decrease in endogenous release of insulin [11]. The antidiabetogenic effect of Nicotinamide may be due to an increase in the pool size of NAD^{++} in beta-cells. The principal metabolite of Nicotinamide is NAD^{++}. It appears that the pool size of NAD^{++} in beta-cells in pre-diabetics and diabetics is significantly reduced. Damage and destruction of beta-cells may occur via oxidative stress. Increased levels of reactive oxygen species in beta-cells may result in, among other things, oxidative damage to DNA resulting in DNA strand breaks [12, 13]. Glibenclamide, a second generation sulfonylurea stimulates insulin release from pancreatic cells. The acute administration of sulfonylureas to type 2 Diabetes patients increases insulin release from the pancreas. Glibenclamide also may further increase insulin levels by reducing hepatic

clearance of the hormone. The antihyperglycemic effect of Carica seed extract may be either due to enhanced secretion of insulin from the beta cells of pancreas or may be due to increased tissue uptake of glucose. The abnormal high concentration of serum lipids mainly due to the increase in the mobilization of frees fatty acids from the peripheral fat deposits, because insulin inhibits hormone sensitive lipase production. However, administering Carica seed extract in the dose of 100 and 200mg/kg body weight to diabetic rats brought the values near to normal level in a dose dependent manner. Thus Carica seed extract exhibited hypocholesterolaemic, hypotriglyceridaemic effects along with decline in blood glucose levels. The active constituents of the plant responsible for the hyperglycemic and hypolipidemic activity are not known. However, some studies have reported that the presence of flavonoids, alkaloids and tannins in the plant extract might be responsible for the biological activity [21]. Again, these studies would require experimental validation. Since most of the antidiabetic drugs do not correct abnormal lipid levels, the observed hypolipidemic activity of this plant extract in diabetic rats makes *Carica papaya* quite important in the management of diabetes. Further investigations are needed to elucidate the mechanism of action of the bioactivity-guided fractionation, enzymatic study of the constituents and isolation identification of the plant extract responsible for the observed pharmacological activities.

5. CONCLUSION

From our study, obtained results showing that the aqueous extract of *Carica papaya* seeds possess antidiabetic and antihyperlipidaemic activities in the Streptozotocin - Nicotinamide induced Type 2 diabetic rats.

6. REFERENCES

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