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Lipid-lowering effect of aqueous leaf extract of Carica papaya on alloxan monohydrate induced male diabetic albino mice

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ABSTRACT

Carica papaya leaf is considered extensively in the indigenous system of medicine as an antidiabetic agent. The current investigation focuses attention on the lipid-lowering property of the aqueous extract of Carica papaya leaves on chemically induced diabetes in albino mice. The lipid parameters studied are plasma total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), very low-density cholesterol (VLDL-C), triglyceride (TG) and phospholipids (PL). The aqueous extract of C. papaya (250 mg/kg) reduced the total cholesterol of normal mice from 92.69±2.14 to 78.92±2.01 mg/dl 8 weeks after oral administration of the extract (P<0.05). It also significantly lowered triglycerides level from 168.32±2.17 to 115.43±4.34 mg/dl, and lowered phospholipids level in diabetic mice from 126.00±2.25 to 89.86±2.38 mg/dl.

***Keywords*:** *Carica papaya alloxan monohydrate, Diabetes mellitus, Hyperlipidemia*

1. INTRODUCTION

Diabetes mellitus is a syndrome characterized by depleted insulin secretion, hyperglycemia and altered metabolism of lipids, carbohydrates and proteins (Davis et al., 1996). A number of pharmacological and chemical agents act as diabetogenic and produce variety of diabetic complications. Alloxan monohydrate induction of diabetes is an experimental model widely used to study glycemic and lipidemic changes in plasma.

Many species of plants and herbs are known to act as anti-diabetic agents, but only a few of them have been investigated (Gupta, 1994). Some plant based therapies attract much interest as they are effective in reducing lipid levels (Kamesh and Sumathi, 2012). The treatment for hypercholesterolemia and Cardio Vascular Diseases with medicinal plants has increased and seems to produce minimum adverse side effects (Ray et al., 2014). Several reports have shown that herbal medicine reduces lipid peroxidation in blood, has anti-cancer activity in vitro and it is useful for treating infectious disease (Otsuki et. al,2010).Herbal medicine is widely used by the population from developing countries, but few scientific studies have explored the safety and efficacy of these traditional remedies (Cholesterol Treatment Trialists- CTT, 2015).In this way, the *C. papaya* leaves have been used as a remedy for various disorders including cancer and infectious diseases (Davis et. al, 1996). Moreover, *C. papaya* leaf methanol extract showed a HDL-C raising effect that improving the CVD risks (Joerin et. al, 2014). However, to our knowledge, no report of its hypolipidemic effect has been published. The objective of this study was to evaluate the hypolipidemic action of Carica papaya extract and its action on liver metabolic parameters of hypercholesterolemic mice.

Carica papaya leaves (family- Caricaceae), popularly known as papita leaf is a medicinal plant that grows throughout the greater parts of India. This plant is widely cultivated for its edible pleasant fruit, which provides good nutritional value and easy digestion (Das et. al, 1999). The leaves is known to possess anti-inflammatory, anti-dysenteric, antioxidant, antidiabetic and diverse pharmacological properties (Isela et. al, 2014). Several studies also shown that its leaf decreased blood glucose significantly in

different animal models (Azuma et. al, 2006). *Carica papaya* leaves have been shown to prevent hyperglycemia and pancreatic damage induced by alloxan monohydrate in mice (Shanmugasundaram et al., 1999). Dietary supplement with *Carica papaya* leaves has been shown to reduce total serum cholesterol, LDL + VLDL, increased HDL, decreased the release of lipoproteins into circulation and increased catalase activity in mice (Pochapski et. al, 2011).

The present study was carried out in swiss albino mice to explore the effects of *Carica papaya* aqueous leaf extract on changes in plasma lipid profile associated with diabetes.

2. MATERIALS AND METHODS

Plant material

Leaves of *Carica papaya* were collected fresh from plants grown in University Department of Botany campus, Bhagalpur, Bihar, India. Taxonomic identification was authenticated by the University Department of Botany, T.M Bhagalpur University, Bhagalpur, and Bihar, India. The leaves were air dried, reduced to powder and were kept separately in airtight containers until the time of use.

Preparation of aqueous extract

Powder of *Carcia papaya* leaves (100 g) was taken and 200 ml of distilled water was added and boiled then filtered off by using Whatman's filter paper No.-41. The final concentration of the extract was 150 mg/ml. The filtrate obtained served as crude extract and administered orally into the experimental animals at the concentration of 150 mg/kg body weight per day for 8 weeks. (Pochapski et. al, 2011)

Test Animals

Experimental animals and Induction of diabetes. Adult male Swiss albino mice (25-30 g) bred in the Animal House, University Department of Zoology Sciences campus, T.M Bhagalpur University, Bhagalpur were used in this study. The animals were housed in polypropylene cages under controlled conditions of 12-h light/dark cycle, and at 24°C. They were maintained on standard diet containing 22% protein, 4.28% oil, 3.02% fiber, 7.8% ash and 1.3% silica (Amrit Laboratory Animal Feed, Nav Maharashtra Chakan Oil Mill Ltd, Pune, India) and water ad libitum (Zarrow et. al, 1964). Diabetes was induced in mice by intra peritoneal injection of 100 mg/kg body weight of alloxan monohydrate (5% w/v), freshly dissolved in physiological saline immediately before use (Dunn and Mcletchie, 1943).The diabetic state was confirmed 48 h after alloxan monohydrate injection by weight loss, glucosuria and hyperglycemia). The animals, which presented blood glucose level above 200 mg/dl, as well as with the clinical signs of polydypsia, polyuria and polyphagia, were selected for the experiment (Jennings et. al, 1983 and Sacs, 1997)

Treatment

Test Animals were divided into following 3 groups containing 6 mice in each group.
Group I: Normal mice received only physiological saline,
Group II: Control diabetic mice received only physiological saline,
Group III: Diabetic mice received aqueous extract of Carica papaya leaves (150 mg/kg body weight) per orally daily.
This study was carried out for 8 weeks according to the guidelines of the Institutional Animal Ethical Committee. Animals were anaesthetized with ether after which blood from retro orbital venous plexus was collected for estimation of plasma lipid profile (Dacie and levis, 1975).

Biochemical analysis

Plasma TC (Allain et. al, 1974), HDL-C (Allain et. al, 1974) and TG (Footsati and Prencipe., 1982) estimation were carried out using respective diagnostic commercial kits from Accurex Biomedical Pvt. Ltd., Bombay, India. Phospholipids (Ackermann and Toro., 1963) level was estimated in plasma. VLDL-C and LDL-C in plasma were also calculated as per Friedewald's equation (Fridewald et. al, 1979).
Statistical analysis the results were expressed as mean ± SEM.
Statistically analysis was carried out using one-way ANOVA below $P<0.05$ implied significance (Theodar and Pollak, 1968).

3. RESULTS AND DISCUSSION

Table-1 and 2. Shows the effect of oral administration of aqueous extract of *Carica papaya* leaves on plasma lipids. The mice of Group- II, diabetic control showed a marked increase in plasma TC, LDL-C, VLDL-C, TG and PL and a fall in HDL-C levels when compared to normal control group. However, following treatment with aqueous extract of *Carica papaya* (600 mg/kg) for 8 weeks, the plasma TC, LDL-C, VLDL-C, TG and PL were reduced significantly ($P<0.05$), while HDL-C remains unchanged in extract treated group when compared Studies in human and animals demonstrated that alteration of blood lipid profiles in condition of diabetes represents a risk factor for cardiovascular diseases (Biosca et. al, 1992). A number of pharmacological and chemical agents act as diabetogenic and produce variety of diabetic complications. Alloxan monohydrate monohydrate induction

of diabetes is an experimental model widely used to study glycemic and lipidemic changes in plasma (Dunn and Maclechate, 1943).

Previous study demonstrated that aqueous extract of Carica papaya had a hypoglycemic effect in diabetic mice (Isela et. al, 2014). The present study evaluated the effect of Carica papaya aqueous leaf extract on lipid parameters such as plasma TC, LDL-C, VLDL-C, HDL-C, TG and PL in alloxan monohydrate-induced experimental diabetic mice (Pedro et. al, 2016).

Following the treatment with alloxan monohydrate to mice a remarkable rise in the levels of plasma TC, LDL-C, were observed. Previous reports suggest that, elevated TC and LDL-C levels in the plasma of diabetic are considered to be a prime cause of coronary heart disease (CHD) (Rodrigues and McNeil, 1986). Many epidemiological studies showed that drug or diet induced reduction of TC and LDL-C could reduce the risk of CHD (Levine et. al, 1995). In the present study, its recovery towards normal levels in aqueous extract administered diabetic mice coincides with the above observations, thus unearthing the cardioprotective effect of Carica papaya leaves. The TG, PL and VLDL-C content in plasma registered a significant hike in diabetic control group, which was retrieved to near normalcy in aqueous extract treated diabetic mice. This observation also indicates the lipid lowering potential of *Carica papaya* (Sasidharan et. al, 2011).

Phytochemical analysis of *Carica papaya* leaf shows the presence of alkaloids, flavonoids, glycosides, minerals, vitamins and many other compounds (Juárez-Rojop et. al, 2012). It has been reported the effect of tertiary and quaternary alkaloids, flavonoids and glycoside components reduces lipid levels in animals (Otsuki et. al, 2010).

The varied chemical composition found in this leaf extract assigns to its lipid lowering property. This property of *Carica papaya* leaf extract may also be because of its other properties like anti inflammatory property which may prevent inflammatory pancreatic damage, immunomodulating property and antioxidant property (Alarcon-Aguilara et. al,1998) thereby reducing the oxidative stress imposed by the chemicals (alloxan monohydrate); this antioxidant mechanism seems to be important as *Carica papaya* leaves has been shown to reduce oxidative stress and oxidative stress has been found to be the most (Indran et. al,2015).

In conclusion, this study has shown that, oral administration of the aqueous extract of *Carica papaya* leaves have significantly reduced plasma lipid levels associated with diabetes mellitus. Thus it can be concluded that extract of *Carica papaya* leaves prevents as well as reverse the plasma lipid profile, thus emphasizing the protective role against diabetes induced hyperlipidemia. Further studies on the active components of *Carica papaya* and mechanism of its protective effect against diabetic hyperlipidemia are needed.

Table 1: Effect of aqueous extract of Carica papaya on the lipid profile of chemically induced diabetic male albino mice

Treatment group	TC	TG	PL
Group I	70.38 ±0.82	78.58 ±1.35	74.75 ±1.07
Group II	92.69 ±2.14*a	158.52 ±2.17*a	126.00±2.25*a
Group III	78.92 ±2.01*b	115.48 ±4.54*b	89.86 ±2.38*b

Table 2: Effect of aqueous extract of Carica papaya leaves on the lipid profile of chemically induced diabetic male albinomice

Treatment group	LDL-C	HDL-C	VLDL-C
Group I	24.19 ±1.30	44.38 ±0.76	18.96 ±0.64
Group II	29.21 ±1.24*a	35.72 ±0.56*a	30.24 ±0.63*a
Group III	26.18 ±1.42*b	29.92 ±0.43	25.84 ±1.37* b

The values are expressed in mg/dl. Values are expressed as mean ± SEM for six animals in each group.
**a values are significantly different from normal control (Group I) mice.*
**b values are significantly different from diabetic control (Group II) mice.*
Bonferroni's test (<0.05) was used; Group I (normal control mice), Group II (diabetic control mice), Group III (aqueous extract treated diabetic mice), TC - total cholesterol, TG - triglycerides, PL - phospholipids, LDL-C - LDL-cholesterol, HDL-C - HDL-cholesterol, VLDL-C - VLDL-cholesterol

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