



ANTIDIABETIC ACTIVITY OF *CINNAMOMUM MACROCARPUM* HOOK.F.LEAVES ON ALLOXAN- INDUCED DIABETIC SWISS ALBINO MICE

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ABSTRACT: The effect of ethanolic extract of *Cinnamomum macrocarpum* (CM) leaves on the functions of hyperglycemia, protein and serum marker enzymes were evaluated in Alloxan induced diabetic male Swiss Albino mice. After 15 days of administration of CM extract at an oral dose of 100 mg/kg body weight, significant increase in the levels of blood glucose in group II and decrease in the blood glucose level in group III, IV and V were observed. A decrease in the activities of serum protein, HDL and triglycerides in group II diabetic mice and these levels were increased in CM treated group III and IV. The marker enzymes SGPT, SGOT and ALP levels were significantly increased in group II animals and decreased in Alloxan treated groups and compared to normal. The groups treated with CM extracts showed significant decrease in the serum marker enzymes. The antidiabetic effect of CM extract was compared with the standard antidiabetic drug, glibenclamide.

Key words: *Cinnamomum macrocarpum*(CM), Hyperglycemia, Alloxan, Glibenclamide

INTRODUCTION

Diabetes mellitus is one of the most challenging metabolic disorders of the 21st century that affects essential biochemical pathways in the body such as carbohydrate, protein and lipid metabolism [1]. Diabetes mellitus is a disease that occurs when the body does not have the hormone insulin or cannot use insulin properly. Dyslipidemia is a metabolic abnormality of body fat. Glucose cannot be used as a source of energy so that the energy obtained from the breakdown of fat (lipolysis). Activity lipolysis (breakdown of fat) causes controlled high levels of free fatty acids, triglycerides (hypertriglyceridemia) and cholesterol (hypercholesterolemia) can trigger the risk of cardiovascular complications such as atherosclerosis [2]. According to the World Health Organization (WHO), up to 90% of the population in developing countries uses plants and its products as traditional medicine for primary health care [3]. It is reported that about 21,000 plants are having medicinal properties and of which, about 800 plants have been reported to show antidiabetic potential [5].

Combination of aqueous extracts of roots and leaves (200 mg/kg body wt) of *A. augusta* (*Abroma*) and *A. indica* (*Azadirachta*) respectively was administered orally to Alloxan diabetic rats once a day for a week. This treatment caused significant lowering of blood sugar and lipids during fasting as estimated by glucose tolerance test [6].

Comparison of blood sugar lowering activity of aqueous extracts of four medicinal plants *Azadirachta indica*, *Gymnema sylvestre*, *Catharanthus roseus* and *Ximium sanctum* showed varying degrees of reduction in blood sugar level using as a rat diabetic model, and it was found that *A. indica* leaf extract exhibited the most potent blood sugar-lowering activity followed by *C. roseus*, *G. Sylvestre* and *X. Sanctum*. [7].

The oxidative stress induced by Alloxan has been shown to damage pancreatic beta-cell and produce hyperglycemia in rats. The activity of leaf extract of *Aegle marmelos*, which is being used in Ayurveda as a medicine for diabetes, was examined for anti-diabetic as well as the antioxidant effects in experimental rat and it was shown that the extract effectively reduced the oxidative stress induced by Alloxan while exhibiting blood sugar lowering potential [8].

The extracts of many plants have become popular in recent years and attempts to characterize their bioactive principles have gained momentum for varied pharmaceutical and food processing applications. *Cinnamomum macrocarpum* plants have antioxidant and antimicrobial activity. The plant has been reported for its antimicrobial properties [9] and there is no report on antidiabetic potential from *Cinnamomum*. In this study, we attempted to study the antidiabetic effect of CM extract in comparison with the standard antidiabetic drug, glibenclamide using mice as an experimental animal.

MATERIALS & METHODS

Plant Material

The fresh leaves *Cinnamomum macrocarpum* were collected from Kolli hills, Nammakal district in the month of January, 2009. The materials were identified and authenticated by taxonomist Rev Fr Dr. John Britto, Rapinart Herbarium, St. Joseph's College, Trichy, Tamil Nadu.

Experimental Plant

Cinnamomum macrocarpum (*Periyalavangapattai*) plant



Figure.1 CM young fresh leaves



Figure.2 CM old leaves & bark

Preparation of Plant Extract

Fresh leaves of the plants were collected, dried separately in an incubator for two days at 40°C, crushed in an electric grinder and powdered. 50 g of the prepared powder was suspended in 300 ml of 70% ethanol and the mixture was filtered and air-dried by low pressure using Soxhlet apparatus. The residue was collected and dissolved in water in a fixed dose and used for the treatment.

Experimental Design

Laboratory inbreds male Swiss Albino mice weighing 25-38 g were obtained from St. Joseph's College, Trichy, India and used for the evaluation of anti-diabetic property of the extract *in vivo*. They were maintained under a constant 12 h light and dark cycle at 22–24°C. The animals were maintained in accordance with the guidelines of the National Institute of Nutrition, Indian Council of Medical Research, and Hyderabad, India. Throughout the experimental period, the animals were fed with a balanced commercial pellet diet and water ad libitum in the animal house.

Experimental Induction of Diabetes

Diabetes was induced by a single dose of Alloxan IP injection (65 mg/kg body weight in 0.9% saline). Diabetes was confirmed in the overnight-fasted rats by measuring blood glucose concentration. When the glucose level is above 250 mg/dl, the mice were considered diabetic and used for further experiments.

Experimental Design

30 adult mice were divided into five groups, five mice each. Group I represented control, Group II diabetic mice (65 mg/kg B.Wt in 0.9% saline), Group III diabetic mice treated orally with CM extract (100 mg/Kg B.Wt.), Group IV mice treated with only CM extract (100 mg/kg B.Wt.) and Group V diabetic mice treated with glibenclamide (200 mg/kg B.Wt) daily for 15 days respectively. The diabetes in mice was induced by alloxan, and the anti-hyperglycemic efficacy of the CM extract was evaluated in diabetic mice. After the experimental period, all the animals were sacrificed by cervical dislocation and biochemical studies conducted in organ samples such as blood, serum and pancreas. The blood and serum samples were assayed for biochemical parameters. Results of the biochemical estimations are reported as mean \pm standard deviation. The significance of the difference between the means of the tests and control studies was established by applying students 't' test for independent samples.

RESULTS

A significant increase in the levels of blood glucose, cholesterol, LDL and VLDL in group II was observed whereas there was a reduction in the levels of these parameters in group III, IV and V. However, serum protein and HDL levels were found to decrease in group II diabetic mice whereas group III and IV showed increased levels of them. When the diabetic and healthy mice treated with CM drug at the dose of 100mg/kg B.Wt, the levels of blood glucose, cholesterol, HDL and VLDL were reduced. The protein levels were increased in the group IV when compared to another 4 groups. It was observed that the CM extract showed anti-hyperglycemic effect in a manner similar to that of reference drug, glibenclamide in Alloxan induced diabetic mice (Table 1).

Table 1: Effect of CM extract on the levels of serum protein, blood glucose, and cholesterol, HDL, LDL and VLDL of normal and diabetic induced adult albino mice against glibenclamide treated diabetic mice.

Parameters	Protein (gm/dl)	Glucose (mg/dl)	Cholesterol (gm/dl)	HDL (gm/dl)	LDL (gm/dl)	VLDL (gm/dl)
Group I	53.38 \pm 6.56	53.38 \pm 6.56	80.84 \pm 41.19	39 \pm 1.84	13.20 \pm 7.73	9.2 \pm 0.16
Group II	55.28 \pm 7.15 ^{a***}	55.28 \pm 7.15 ^{a***}	182.98 \pm 7.89 ^{a***}	27.5 \pm 2.88 ^{a***}	25.3 \pm 6.81 ^{a***}	13.2 \pm 0.46 ^{a***}
Group III	82.12 \pm 35.36 ^{b*}	82.12 \pm 35.36 ^{b*}	52.83 \pm 4.1 ^{b***}	49.12 \pm 12.20 ^{b***}	22.6 \pm 0.23 ^{b*}	8.1 \pm 1.96 ^{b*}
Group IV	130.1 \pm 3.54	130.1 \pm 3.54	102.77 \pm 23.84	46 \pm 3.27	16.2 \pm 8.49	8.8 \pm 0.69
Group V	48.85 \pm 1.26	48.85 \pm 1.26	163.24 \pm 13.22	51 \pm 5.77	21.4 \pm 0.37	9.3 \pm 1.27

The values are expressed as Mean \pm SEM (from 6 experiments from each group) Comparison between a-Group I & Group II; b-Group II & Group III. * (p<0.01), ***(p<0.0001).

Table 2 shows the effect of CM extracts on serum Triglycerides, SGOT, SGPT and ALP of normal and diabetic induced adult albino mice against glibenclamide treated diabetic mice. A decrease in the activities of serum triglycerides in group II diabetic mice was observed, and on contrary, these levels were increased in CM treated group III and IV. The levels of marker enzymes such as SGPT, SGOT and ALP were found to be significantly elevated in the Alloxan treated groups when compared to normal. The groups treated with CM extracts showed significant decrease in the serum marker enzymes. The antidiabetic effect of CM extract was compared with a standard antidiabetic drug, glibenclamide.

Table 2: Effect of CM extracts on serum Triglycerides, SGOT, SGPT and ALP of normal and diabetic induced adult albino mice against glibenclamide treated diabetic mice.

Parameter	Triglycerides (gm/dl)	SGOT (u/l)	SGPT (u/l)	ALP (u/l)
Group I	150.75±3.62	58.81±8.69	26.13±8.35	55.73±19.09
Group II	87.52±14.81 ^{a***}	113.28±8.72 ^{a**}	29.18±4.46 ^{a***}	125.12±41.65 ^{a**}
Group III	136.7±1.35 ^{b***}	65.22±5.04 ^{b***}	24.33±6.07 ^{b***}	59.54±10.45 ^{b*}
Group IV	108.71±5.63	118.23±23.84	40.18±2.59	58.78±36.57
Group V	101.12±18.47	70.35±6.90	19.18±1.95	69.07±22.36

The values are expressed as Mean ± SEM (from 6 experiments from each group) Comparison between **a**-Group I & Group II; **b**-Group II & Group III.

*($p < 0.01$), ***($p < 0.0001$), **($p < 0.001$).

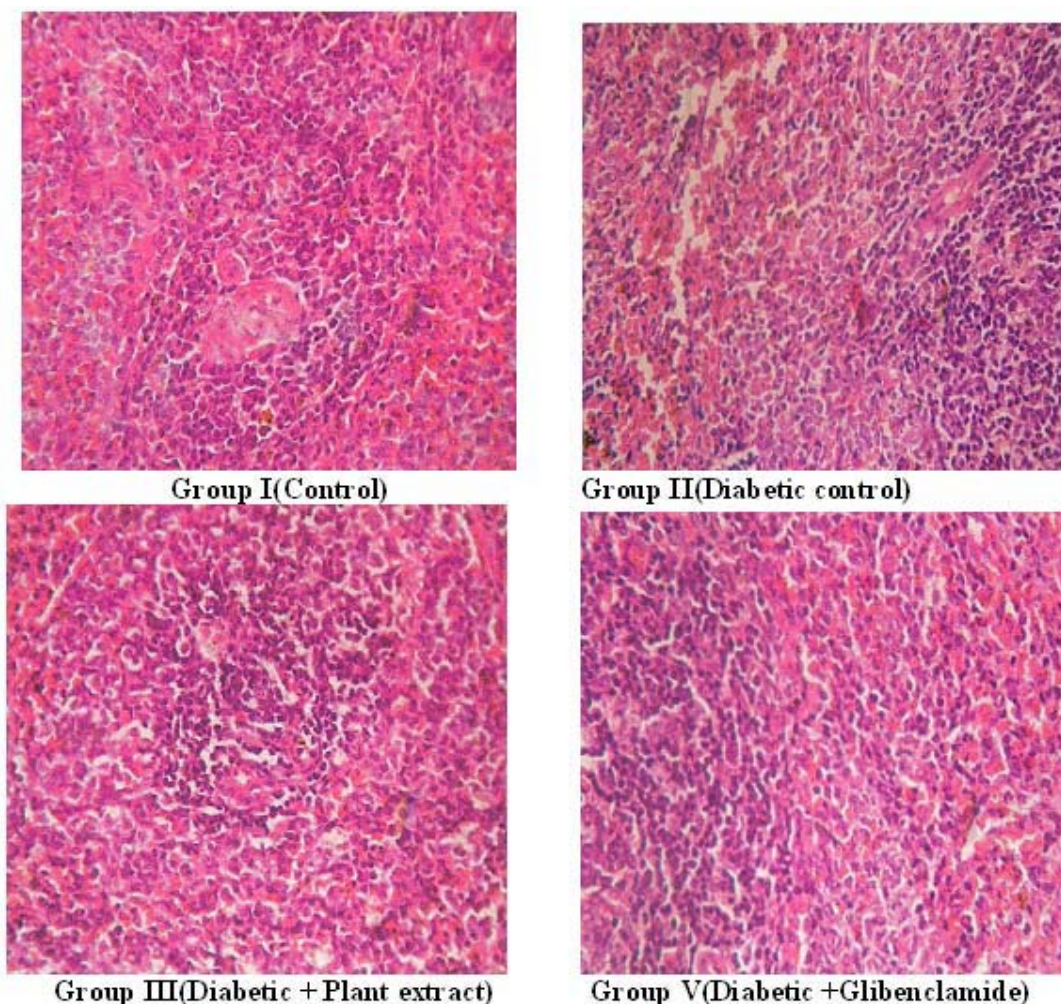


Fig. 3 Histopathology of Pancreas

DISCUSSION

Diabetes is manifested by multiple disturbances in the metabolic processes of the body, which are directly attributed to insufficient supply of insulin [10]. Alloxan administration in experimental animals has been reported to produce pancreatic lesion which is proportional to the dose of the drug administered, and the size of the lesion also correlates with the pancreatic insulin content [11]. This perhaps explains why the drug at a low or medium dose does not produce absolute but insufficient insulin deficiency in experimental animals. Therefore the experimental dose of the drug must be carefully selected in order to avoid excessive pancreatic tissue damage. The most frequently used intravenous dose of Alloxan in rats is 65 mg/kg, but when it is administered intraperitoneally or subcutaneously its effective dose must be higher [12].

Alloxan, a beta cytotoxic, destroys β - cells of islets of Langerhans of pancreas, resulting in a decrease in endogenous insulin secretion and paves ways for the decreased utilization of glucose by body tissue. It results in elevation of blood glucose level, decreased protein content, increased levels of cholesterol and triglycerides [13].

In the previous study a number of plants have been used traditionally in treatment of diabetes and some have been proven scientifically to have hypoglycemic activity. These plant extracts contain compounds such as polysaccharides [14], flavonoids [15], terpenoids and tannins [16], steroid [17], polypeptides [18] and alkaloids [19], and these compounds are responsible for the antidiabetic activity. The higher blood glucose levels are expected in Alloxan induced diabetic mice. Since Alloxan causes a massive reduction in insulin release due to the destruction of cells of the islets of Langerhans and thereby induces hyperglycemia [20].

The effect of *Azadirachta indica* leaf extract on changes in serum lipid profile in streptozotocin induced diabetic rats was studied with a view to elucidate its possible effect on cardiovascular disease induced by hyperglycemia. It was observed that *A. indica* leaf extract significantly reduced the total cholesterol, LDL, VLDL, triglycerides and total lipids in serum of streptozotocin induced diabetic rats but HDL levels remained unchanged [21]. In our present study the *Cinnamomum macrocarpum* leaves shows presence of steroids, Alkaloids, Tannin, saponins & flavonoids. Present study elicited a significant increase in the activities of protein, HDL-C, triglycerides, in group III animals and decreased in II animals when compared to control group. A significant increase in the glucose, cholesterol, LDL-C, VLDL-C, in group II animals and decreased in group III animals when compared to control group. Since the changes associated with diabetic rat liver damage are similar to that of acute viral hepatitis [22], diabetic mediated hepatotoxicity was taken here as the experimental model for liver injury. The hepatotoxic compounds such as STZ are known to cause marked elevation in serum transaminases. In agreement with results obtained in previous investigations [23,24], In our study SGOT, SGPT, ALP is significantly increased in group II animals and decreased in group III animals when compared to control group. Histology of the pancreas the normal rat showed normal pancreatic islets cells. Pancreas of untreated diabetic control rat showed atrophy with degeneration and necrosis of pancreatic tissue and invasion of connective tissues in the parenchyma of pancreatic islets. *Annona squamosa* Linn extract-treated diabetic rat showed slight regeneration of pancreatic cells with normal islet cells. The pancreas of glibenclamide-treated diabetic rat revealed partial regeneration of islet cells with presence of numerous beta cells in pancreatic islets [25]. In our study, CM treated diabetic rats showed regeneration of the pancreatic β cells with normal islet cells and the effect was comparable to that of glibenclamide-treated diabetic rats.

In conclusion, *Cinnamomum macrocarpum* leaves extract showed anti-hyperglycemic effect in a manner similar to that of reference drug, glibenclamide in Alloxan induced diabetic mice. The extracts also exhibited reduction in serum markers, triglycerides and LDL while showing anti-diabetic effect.

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