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ANTIDIABETIC ACTIVITY OF METHANOL EXTRACT OF *Coriandrum sativum* Linn FRUIT

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ABSTRACT
Diabetes mellitus is a metabolic disorder characterized by disturbances in carbohydrate, protein and lipid metabolism and by complications like micro vascular (retinopathy, neuropathy and nephropathy) and macro vascular (heart attack, stroke and peripheral vascular disease) complications. In the present study diabetes was induced in albino rat models with streptozotocine. *Coriandrum sativum* Linn, has been claimed to possess antidiabetic properties in Traditional System of Medicine. The present study was undertaken to screen the hypoglycemic activity of 75% methanol extract of fruits of *Coriandrum sativum*. The 75 % methanol extract showed significant decrease in blood glucose level at a dose of 100 mg/kg and 200 mg/kg. It also decreased the lipid parameters such as total cholesterol, total triglycerides, total bilirubin, SGOT,SGPT and SALP when compared with diabetic control. 75% methanol extract at 100 mg/kg was better in controlling diabetes when compared to 200 mg/kg bw suggesting that *C.sativum* to possess antidiabetic activity.

KEYWORDS: *Coriandrum sativum*, Diabetes mellitus, Streptozotocine, Blood glucose, Lipid profile.

INTRODUCTION
Diabetes mellitus is a metabolic disorder characterized by disturbances in carbohydrate, protein and lipid metabolism and by complications like micro vascular (retinopathy, neuropathy and nephropathy) and macro vascular (heart attack, stroke and peripheral vascular disease) complications.[1] A world wide survey has reported that diabetes mellitus affects nearly 10% of the population. It has been predicted that the prevalence of diabetes in adults will increase from 135 million in 1995 to 350 million in 2030 as given by International Diabetes Federation.[2,3] Currently available synthetic antidiabetic agents produce serious side effects like hypoglycemic coma and hepatorenal disturbances.[4,5] Patients are therefore using herbal medicines which have fewer side effects and have the potential to impart therapeutic effect in complicated disorders like diabetes and its complication.[6] Following the WHO's recommendation for research on the beneficial uses of medicinal plants in the treatment of diabetes mellitus, investigations on hypoglycemic agents derived from medicinal plants have also gained momentum. Traditional medicinal plants with various active principles and properties have been used from ancient times by physicians and laymen to treat a great variety of human diseases such as diabetes, coronary heart disease and cancer. Antidiabetic agents from medicinal plants could serve as a good source for drug design and much attention has been fixed on formulation of herbal medicine.[7]

Plants are well known in traditional herbal medicine for their hypoglycemic activities and available literature indicate that there are more than 800 plant species showing hypoglycemic activity. There has been increasing demand for the use of plant products with antidiabetic activity due to low cost, easy availability and lesser side effects. Therefore, plant materials are continuously scrutinized and explored for their effect as hypoglycemic agents. One such plant is *Coriandrum sativum* which has been used in traditional system of Indian medicine for treating diabetes.

Coriander [*Coriandrum sativum* Linn.] an annual of the Apiaceae family is one of the valuable medicinal and seasoning plant. This species comes from the Mediterranean region and it is grown all over the world. The coriander fruit and essential oil isolated from it are used for medicinal purpose.[8,9] *C. sativum* is widely used in traditional medicine to treat anxiety, dizziness, headache, edema, fever, digestive disorders, respiratory diseases, allergies, and burns.[10,11] The fruits are used as astringent, anthelmintic, emollient, stomachic, antibilious, digestive, appetizer, constipating, diuretic, antipyretic, refrigerant, tonic, expectorant, anodyne, antidiabetic and dyspepsia. The phytochemical screening of *Coriandrum sativum* showed that it contained essential oil, tannins, terpenoids, reducing sugars, alkaloids, phenolics, flavonoids, fatty acids, sterols and glycosides. It also contained high nutritional values

including proteins, oils, carbohydrates, fibers and wide range of minerals, trace elements and vitamins. The previous pharmacological studies revealed that it possessed anxiolytic, antidepressant, sedative-hypnotic, anticonvulsant, memory enhancement, improvement of orofacial dyskinesia, neuroprotective, antibacterial, antifungal, anthelmintic, insecticidal, antioxidant, cardiovascular, hypolipidemic, anti-inflammatory, analgesic, antidiabetic, mutagenic, antimutagenic, anticancer, gastrointestinal, deodorizing, dermatological, diuretic, reproductive, hepatoprotective, detoxification and many other pharmacological effects.[12-17]

Silver nanoparticles were synthesized using methanol and aqueous extract of fruit of *C.sativum* and its antioxidant activity were reported.[18] We have reported better activity with 75% methanol extract of fruit of *C.sativum* and HPTLC data also showed that 75 % methanol extract has more number of phytoconstituents than all other extract. In the light of the above information, the present investigation was under taken to evaluate the antidiabetic activity using streptozotocine[STZ] induced diabetic rat model.

MATERIALS AND METHODS

Plant material

The *Coriandrum sativum* fruits were collected from local market in Bangalore, Karnataka, India and it was identified and authenticated by Botanist, Natural Remedies Pvt Ltd., Bangalore. A voucher specimen was deposited in The Oxford College of Pharmacy, Bangalore. The fruits were dried in shade and powdered coarsely, passed through sieve no. 40 and stored in air tight container for further use.

Preparation of fruit extract

Coarsely powdered fruits of *C.sativum* 200 g was extracted with 75% methanol [1500 ml] in soxhlet apparatus till the complete exhaustion, filtered. The methanol extract was concentrated by rotary vacuum evaporator and evaporated to dryness.

Chemicals used The streptozotocine was procured from Hi-Media and all other chemicals and solvents used were of analytical grade.

Animals

Mature Albino rats obtained from the Animal house of The Oxford College of Pharmacy, Bangalore were used for the studies. Rats were maintained under standard conditions (27 ± 2°C; relative humidity 60 ± 5 %, light dark cycle of 12 hrs) and fed with standard pellet diet and water *ad libitum*. Prior to the experiment the animals were fasted for 12 h with water *ad libitum* given and weighed. All procedures described were reviewed and approved by Institutional Animal Ethics Committee.

Acute Toxicity Study

The toxicity study reveals the safety of *Coriandrum sativum* in Rat. There was no marked change in the general behavior up to 2000 mg/kg., body weight of *C.sativum*. No mortality was observed during the observation period as per literature study.[19]

Antidiabetic Activity

Antidiabetric activity of *C.sativum* were determined by Streptozotocine induced diabetes mellitus model.[20]

Induction of Diabetes

The animals were fasted for 16 hour prior to the induction of diabetes. STZ freshly prepared in citrate buffer (pH 4.5) was administered i.p. at a single dose of 50 mg/kg. Development of diabetes was confirmed by polydypesia, polyurea and by measuring blood glucose concentrations 72 hour after injection of STZ. Rats with blood glucose level of 250 mg/dl or higher were considered to be diabetic and selected for experiment.

Experimental Design

Animals were divided into five groups, each consisting of six rats. The extracts were administered for 14 days.
Group 1: Normal rats received only vehicle (Normal control)
Group 2: Streptozotocine induced rats received only vehicle (Diabetic control)
Group 3: Streptozotocine induced rats received Glibenclamide (0.5 mg /kg) daily for 14 days. Group 4: Streptozotocine induced rats received lower dose (100 mg /kg body wt. p.o) as CS1. Group 5: Streptozotocine induced rats received higher dose (200 mg/kg body wt .p.o) as CS2.

Testing of fasting blood glucose level and biochemical parameters

Fasting blood glucose levels were measured on 0, 7, and 14 days of treatment of all these groups. Blood was collected from tip of the tail vein and fasting blood glucose level was measured using single touch glucometer. The results were expressed in terms of milligram per decilitre (dL) of blood. The body weight of each animal was noted. At the end of the experimental period, all the animals were sacrificed by decapitation and blood was collected with anti-coagulant and the serum was used for the estimation of various biochemical parameters like cholesterol, total triglycerides[TG], total bilirubin[TB], SGPT,SGOT and ALP by using kits obtained from M/s Unitronic Pvt Ltd.

STATISTICAL ANALYSIS

The results are expressed as mean ± S.E.M. Statistical difference was tested by using one-way analysis of variance (ANOVA) followed by Dunnet's test. Values are expressed as mean ± SEM (n=6) in each group. **Values are significantly different from hyperglycemic control at $p < 0.01$. * Values are significantly different from hyperglycemic control at $p < 0.05$

RESULTS AND DISCUSSION

The effect of repeated oral administration of 75% methanol extract of the fruits of *Coriandrum sativum*

(CS) on blood glucose levels in streptozotocine induced diabetic rats is presented in Table-1. Effect of 75 % methanol extract of the fruits of *Coriandrum sativum* (CS) on Hepatic enzymes and lipid profile are given in Table-2.

Treatment with methanol extract of *C.sativum* fruits at the dose of 100 and 200 mg/ kg body weight for 1st and 2nd week exhibited a significant ($p<0.05$) decrease in the fasting blood glucose in streptozotocin induced diabetic animals as compared to diabetic control (Table-1). Blood glucose level of diabetic animals started decreasing from the first week of drug treatment that was continued to maintain till 2nd week, which was comparable to glibenclamide 0.5 mg/ kg.

The efficacy of CS1 and CS2 at the dose of 100 mg/kg and 200 mg/ kg on serum SGOT, SGPT, ALP, total bilirubin, TG and total cholesterol in diabetic rats was evaluated. The above biochemical parameters were significantly ($p<0.01$) altered in STZ induced diabetic rats compared to normal control rats. In diabetic rats, administration of CS1, CS2 and glibenclamide significantly ($P< 0.01$) reduced SGOT, SGPT, ALP,TG, total bilirubin and total cholesterol level compared to diabetic control rats (Table-2).

In light of the results, our study indicates that fruits of *Coriandrum sativum* Linn have significant antihyperglycemic activities in Streptozotocin (STZ) induced hyperglycaemic rats. They can also improve the condition of diabetes as indicated by parameters like lipid and biochemical parameters. Streptozotocin was known to destroy the β-cells of the pancreas, which causes selective pancreatic islet β-cell cytotoxicity mediated through the release of nitric oxide (NO), methyl cations, methyl radicals, reactive oxygen species (ROS). This results in rapid reduction in pancreatic islet pyridine nucleotide concentration and subsequent β-cell necrosis. The action of STZ on mitochondria generates SOD anions, which leads to diabetic complications.[21-23] Sulfonylureas such as glibenclamide are often used as a standard antidiabetic drug in STZ-induced diabetes to compare the efficacy of variety of antihyperglycemic compounds. It has been involved in stimulating insulin secretion from pancreatic β-cells principally by inhibiting ATP sensitive KATP channels in the plasma membrane. In our study, there was a significant elevation in blood glucose level in diabetic control group as compared with normal animals. The CS1 and CS2 treated group exhibited significant reduction of fasting glucose levels as compared to the diabetic control group.

The most commonly observed lipid abnormalities in diabetes are hypertriglyceridemia and hypercholesterolemia .[24,25] This might have occurred in the diabetic rats as a result of lack of insulin which activates the lipase enzymes, hydrolyzing the stored TG and releasing large amounts of fatty acids and glycerol in the circulating blood.[26] Consequently, the excess of fatty acids in the plasma may promote the hepatic conversion of fatty acids into phospholipids and cholesterol, the main product of lipid metabolism.[27] The increase level of TG and cholesterol in the blood of diabetic rats may lead to cardiovascular disease. The improvements in the lipid profile in diabetic animals after treatment with CS1 and CS2 could be beneficial in preventing diabetic complications as well as improving lipid metabolism.

Elevation of serum biomarker enzymes such as SGOT, SGPT and SALP were observed in diabetic rats indicating impaired liver function, which is obviously due to hepatocellular necrosis. Diabetic complications such as increased gluconeogenesis and ketogenesis may be due to elevated transaminase activities.[28] Bilirubin is formed from degeneration of haemoglobin by the action of reticuloendothelial systems throughout the body. Increased bilirubin level reflects the depth of jaundice.[29,30] Restoration of these biomarker enzymes towards normal level indicates decreased diabetic complications in CS1 and CS2 treated groups.

Table 1: Effect of 75 % methanol extract of *Coriandrum sativum* fruit in streptozotocine induced diabetes on blood glucose level

Sl. No	Treatment	Blood Glucose (mg/ dl)		
		0 day	7th day	14th day
1	Normal control	90.08 ± 3.21	94.52 ± 3.42	85.11 ± 4.14
2	Diabetic control	290.2 ± 6.46	295.16 ± 4.95	294.23 ± 8.68
3	Standard 0.5mg/ kg	280.78 ± 8.74	234.41 ± 4.89**	213.48 ± 3.44**
4	CS1 100mg/kg	285.21 ± 13.13	237.15 ± 9.91**	215.40 ± 6.48**
5	CS2 200mg/kg	296.86 ± 3.07	240.35 ± 9.56**	222.60 ± 4.34**

Values are expressed as mean ± SEM (n=6) in each group. Values were found out by using one way ANOVA followed by Dunnet's test. **Values were significantly different from hyperglycemic control at $P< 0.01$. '0 day' indicates the initial day in which the treatment commenced.

Table 2: Effect of 75 %methanol extract of *Coriandrum sativum* fruit on biochemical parameter measured in streptozotocine induced diabetes on 14th day

Sl No.	Treatment	Cholesterol (mg/ dl)	TG (mg/ dl)	SGOT (IU/dl)	SGPT (IU/dl)	ALP (IU/dl)	TB (mg/ dl)
1	**Normal control**	39.56 ± 2.05	63.72 ± 4.46	160.56 ± 11.14	125.17 ± 2.91	234.08 ± 12.03	0.65 ±0.07
2	**Diabetic control**	60.78 ± 2.14	93.70 ± 3.14	300.46 ± 15.26	210.30 ± 17.14	296.05 ±20.12	0.40 ± 0.03
3	**Standard 0.5mg/ kg**	35.71 ± 2.78 **	66.75 ± 4.19 **	180.00 ± 12.21 **	125.43 ± 5.98 **	230.35 ± 10.5 **	0.60 ± 0.03 **
4	**CS1 100mg/kg**	39.87 ± 3.18 **	68.95 ± 2.17 **	184.93 ± 7.89 **	128.54± 10.33 **	234.86 ± 0.52 **	0.56 ±0.04 **
5	**CS2 200mg/kg**	44.23 ± 3.47 **	70.14 ± 0.82 **	205.12 ±12.1*	134.29 ±8.72 *	245.06 ± 0.98 *	0.50 ± 0.02 *

Values are expressed as mean ± SEM (n=6) in each group. Values were found out by using one way ANOVA followed by Dunnet's test. **Values were significantly different from hyperglycemic control at $p < 0.01$. * Values were significantly different from hyperglycaemic control at $p < 0.05$.

CONCLUSION

Renewed interest on the use of herbal products is gaining importance. Globally, many herbal products are being used as food supplements for prophylaxis of common ailments such as diabetes, hypertension etc.

Prior to the pharmacological investigation of any herbal product it is mandatory to investigate the safety profile of these herbal products. It is documented that if a herbal substance is free from side effects or adverse effects up to 2000 mg/kg, it is considered safe for clinical use, the absence of acute toxicity is observed thus proving the safety profile of *C.sativum.*

The 75 % methanol extract showed significant decrease in blood glucose level at a dose of 100 mg/kg and 200 mg/kg. It also decreased the lipid parameters such as total cholesterol, total triglycerides, total bilirubin, SGOT,SGPT and ALP when compared with diabetic control. 75% methanol extract at 100 mg/kg was better in controlling diabetes when compared to 200 mg/kg bw suggesting that *C.sativum* possess antidiabetic activity.

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CONFLICT OF INTEREST

None to be declared.

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