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Evaluation of Antidiabetic Activity of Methanolic Leaf Extract of *Coriandrum sativum* in Alloxan Induced Diabetic Rats

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ABSTRACT

Diabetes mellitus is the most common endocrine disorder that impairs glucose homeostasis resulting in severe diabetic complications including retinopathy, angiopathy, nephropathy, and neuropathy causing neurological disorders due to perturbation in utilization of glucose. In the present study diabetes was induced in albino rat models with alloxan monohydrate. *Coriandrum sativum Linn*, has been claimed to possess antidiabetic properties in traditional medicine. The present study was undertaken to screen the hypoglycemic activity of methanolic extracts of leaves of *Coriandrum sativum*. The methanolic extract showed significant dose dependant decrease in blood glucose level at a dose of 200 mg/kg and 400 mg/kg. It also decreased the lipid parameters such as total cholesterol, LDL, HDL, VLDL and TG when compared with diabetic control. Other biochemical parameters such as SGOT and SGPT were found to be dose dependent and were reduced at higher dose of extract.

Keywords: Alloxan, Coriander, Diabetes mellitus, Blood glucose, Lipid profile.

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INTRODUCTION

Diabetes mellitus, or simply diabetes, is a group of metabolic diseases in which a person has high blood sugar, either because the pancreas does not produce enough insulin, or because cells do not respond to the insulin that is produced [1]. Diabetes mellitus is also associated with long-term complications, including retinopathy, nephropathy, neuropathy and angiopathy and several others[2]. Diabetes mellitus (DM) is a multifactorial disease which is characterized by hyperglycemia, lipoprotein abnormalities , raised basal metabolic rate , defect in reactive oxygen species scavenging enzymes and high oxidative stress induced damage to pancreatic beta cells[3].Diabetes mellitus is ranked seventh among the leading causes of death and is considered third when it's fatal complications are taken into account[4]. The World Health Organization (WHO) reported that 300 million peoples world suffer from diabetes mellitus by the year 2025[5]. The search for effective and safer hypoglycaemic agents with a protective effect from diabetic complication has continuous to be a research topic of interest[6]. The World Health Organization has recommended and encouraged the use of alternative therapy especially in countries where access to the conventional treatment of diabetes is inadequate[7]. Plant medicines have a long history as treatment for diabetes with a disturbing rise in the prevalence of this metabolic, disease and associated health care costs, interest in alternative or complementary therapies has grown[8]. Over the two decades , numerous phytotherapies and their combination demonstrate multiple beneficial antidiabetic mechanism, including modulation of carbohydrate metabolism, restoration of beta cell integrity and function, insulin releasing activity , improvement in glucose uptake / utilization antioxidant properties and a redeuction in the risk of cardiovascular disease[7-8] .Plants are well knownintraditional herbal medicine for their hypoglycaemic activities, and available literature indicate that there are more than 800 plant species showing hypoglycaemic activity[9]. 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.

Coriandrum sativum Linn. (Apiaceae) is an annual herb native to Mediterranean region. It is commercially grown in India, Morocco, Hungary, Poland, Romania, Mexico and USA. India is the largest producer of coriander in the world. The fruits are gathered ripe in late summer [10,11]. The fragrant odour and pleasant aromatic taste of coriander is due to the presence of the essential oil which is about 1 per cent in seeds. The chief constituent of oil is (+) linalool (coriandrol)[12]. The fruits are given in spermatorrhoea, leucorrhoea and in rheumatic fever. Dried seeds are reported to possess diuretic and aphrodisiac properties [13]. It has traditionally been referred to as antidiabetic [14], anti-inflammatory and cholesterol lowering [15,16]. It is also reported to have antimicrobial [17,18], anthelmintic [19],antioxidant [20], antifertility [21], antiproliferative [22], anticonvulsant [23], diuretic [24], antiulcer [25], hepatoprotective [26], antifeedent [27], asthmatic [28]and larvicidal activities[29]. The present paper narrates and justify the traditional use of plant with respect to antidiabetic activity and lipid profile of methanolic extract of leaves of *C. sativum* in rats.

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MATERIAL AND METHODS

Plant material

The leaves of *Coriandrum sativum(Linn)* were collected from Greater Noida. The plant was authenticated and identified by Dr. K.C Bhatt (Senior scientist),NBPGR, Pusa Campus, New Delhi and a voucher specimen(NHCP/NBPGR/2013-52) is preserved in our laboratory for future reference. Leaves were shade dried, coarsely powdered, passed through 40 mesh sieve and stored in air tight container.

Preparation of extract

90 gm of the coarsely powdered leaf was passed through 40 mesh sieve and then subjected to extraction with methanol in Soxhlet apparatus. The solvent was removed under vacuum and extract were concentrated to dryness in vacuum and a solid mass (12.5% w/w with respect to dry starting material) was obtained. The methanol extract was stored in a desiccator and used for further experimental studies.

Animals

Albino (Wistar) rats weighing between 200-250 g of either sex were used for antidiabetic activity. All experimental animals were obtained from the animal house, Department of Pharmaceutical Technology, Noida Institute of Engineering and Technology, Greater Noida, and maintained in 25 ± 1°C, with 55 ± 5 % humidity with 12 hr light/dark cycle. The animals were housed in the standard polypropylene cages and provided with food and water ad libitum. The litter in the cages was renewed thrice a week to ensure hygenicity and maximum comfort for animals. Ethical clearance for handling the animals was obtained from the Institutional Animal Ethical Committee prior to the beginning of the project work bearing the protocol number NIET/IAEC/2013/43.

Chemical

Alloxan Monohydrate was purchased from Sigma Aldrich Chemicals Pvt, Ltd, Bangalore. All other chemicals and reagents used were of analytical grade.

Drugs

Standard drug: Glibenclamide, Test drug: Extract of leaves of *Coriandrum sativum.*

Oral acute toxicity studies

Acute toxicity was generally carried out for the determination of LD_{50}value in experimental animals. The LD_{50}determination was done in mice by OECD guidelines 423. The

aim of performing acute toxicity study is for establishing therapeutic index of particular drug and to ensure safety *invivo.*

Antidiabetic Activity

Experimental induction of diabetes

All animals were allowed to adapt to cages for 3 days, after which they were fasted overnight and 120 mg/kg body wt. of alloxan monohydrate freshly dissolved in normal saline was injected intra-peritoneal. Alloxan induces the diabetes by damaging the insulin secreting cells of the pancreas leading to hyperglycemia. After alloxan treatment, all animals were given free access to food and water. Blood glucose levels were measured 2 days after alloxan injection and used as parameters to obtain matching pairs of rats with diabetes of similar level of severity. Only rats with fasting blood glucose levels greater than 140 mg/dl were considered to be diabetic and were used in the experiment.

EXPERIMENTAL DESIGN

Animals were divided into five groups , each consisting of six rats . The extracts were administered for 21 days .

Group 1: Normal rats received only vehicle (Normal control)
Group 2: Alloxan induced rats received only vehicle (Diabetic control)
Group 3: Alloxan induced rats received Glibenclamide (2.5 mg /kg) daily for 21 days.
Group 4: Alloxan induced rats received lower dose (200 mg /kg body wt. p.o) of CSLE.
Group 5: Alloxan induced rats received higher dose (400 mg/kg body wt .p.o) of CSLE.

The values of sample treated were compared with that of the standard group which was treated with Glibenclamide.

Testing of fasting blood glucose level and biochemical parameters

Fasting blood glucose levels were measured on 0, 7, 14, and 21 days of treatment of methanolic extract of leaves of *Coriandrum sativum* Linn to the animals 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 LDL,HDL, VLDL,SGPT,SGOT, TG, TC.

Statistical analysis

All the values were expressed as mean ± SEM (standard error mean) for six rats. Statistical analysis was carried out by using PRISM software package (version 5.0). Statistical

significance of differences between the control and experimental groups was assessed by One-way ANOVA followed by Dunnet's Multiple Comparison Test. The value of probability less than 5% ($P < 0.05$) was considered statistically significant.

RESULTS AND DISCUSSION

Phytochemical analysis

Preliminary phytochemical screening of methanolic extract of leaves of *Coriandrum sativum* showed the presence for alkaloids, flavonoids, coumarins, saponins, sterols and terpenes.

Oral acute toxicity studies

Oral administration of methanolic extract of leaves of *Coriandrum sativum*in mice caused death and behavioural changes at 2000mg/kg body weight (Table.1).LD_{50}value was found to be 1000 mg/kg.

Antidiabetic activity

The effect of repeated oral administration of methanolic extract of the leaves of *Coriandrum sativum* (CSLE) on blood glucose levels in alloxan-diabetic rats is presented in Table- 2 , and the effect on body weight is presented in Table- 3. CSLE, administered at doses of 200 & 400 mg/kg to alloxan-treated diabetic rats caused significant dose related and duration dependent reduction of blood glucose levels. Maximum reduction was observed on day 21. Gradual increase in body weight was also observed. CSLE 400 mg/kg exhibited maximum glucose lowering effect in diabetic rats. Glibenclamide exhibited significant reduction in blood glucose levels at the end of the study when compared to diabetic control.

Estimation of biochemical parameters

CSLE showed a dose related significant reduction in triglycerides compared to pre-treatment levels (Table 4). CSLE at the doses of 200 and 400 mg/kg dose dependently reduced the total cholesterol, LDL, VLDL, TG levels than diabetic control rats.

Table 1: **LD_{50} of methanolic extract of leaves of *Coriandrum sativum***

S.NO	No of animals	Dose	No of death of animals
1	3	5 mg/kg	0
2	3	50 mg/kg	0
3	3	300 mg/kg	0
4	3	2000mg/kg	1

LD_{50} =1000mg/kg ;50 ED_{50}=100mg/kg

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Table 2 : Effect Of CSLE On Blood Glucose Level In Alloxan Induced Diabetic Rats (21 Days Study).

Treatment	Blood Glucose level (mg/dl)			
	0 day	7th day	14th day	21st day
Normal Control	100.534±3.64	100.70±3.49	96.65±2.068	97.52±1.45
Diabetic control (120mg/kg)	253.93±3.86	256.30±5.38*	264.11±6.726*	271.37±2.62*
Glibenclamide (2.5 mg/kg)	251.54±5.06	102.26±3.11**	96.88±2.628**	86.99±1.28**
CSLE(200mg/kg)	251.42±4.25	194.48±4.98**	185.92±3.105**	172.92±5.43**
CSLE(400mg/kg)	248.72±3.80	187.17±4.29**	166.32±1.236**	142.55±2.29**

SEM= Standard Error Mean , All the values are taken as a mean of six animals and expressed as Mean± SEM , when *p< 0.01 significant, **p <0.001 highly significant.

Table 3:Effect of CSLE on body weight in alloxan induced diabetic rats (21day study).

Treatment	0 day	7th day	14th day	21st day
Normal control	202.40±2.74	204±2.77	205.59±2.79	210.12±2.85
Diabetic control (120mg/kg)	202.90.±2.88	173±2.58**	160±2.52**	146±1.71**
Glibenclamide(2.5 mg/kg)	205.92±2.83	203±2.62	197±2.02	191±1.87**
CSLE (200mg/kg)	205±2.38	198±2.13	192±1.87	182.5±1.20**
CSLE (400mg/kg)	206±2.43	199±2.06*	194±1.68*	186±1.48**

SEM= Standard Error Mean ,All the Values are expressed as Mean ±SEM (n=6) ,when *p≤ 0.05 significant, **p ≤ 0.01 highly significant.

Table 4: Effect of CSLE on biochemical parameters measured in alloxan induced diabetic rats (21day study).

Treatmnt	Total cholesterol (mg/dl)	LDL (mg/dl)	HDL (mg/dl)	VLDL (mg/dl)	Triglycerides (mg/dl)	SGOT (IU/L)	SGPT (IU/L)
Nomal control	63.16±1.52	19.97±0.86	27.52±1.14	12.67±0.74	63.35±1.34	15.1±2.3	13.40±2.50
Diabetic control	231.26±5.48	160.47±4.89	48.55±2.43	32.24±1.25*	161.20±4.67*	49.80±1.69	27.8±9.35
Standad (Glibenclamide)	89.49±2.63*	35.5±1.21*	46.67±1.15*	16.32±0.87*	81.6±3.29**	15.3±2.34**	15.3±1.34
CSLE (200mg/kg)	111.42±3.15*	49.73±1.44*	35.15±1.67*	20.54±0.85**	102.7±3.15**	29.1±8.6	22.1±1.84
CSLE (400mg/kg)	98.71±2.14*	35.54±1.46*	43.67±2.18*	17.3±0.61**	93.4±2.68**	18.4±1.96**	13.2±1.47**

SEM= Standard Error Mean ,All the Values are expressed as Mean ±SEM (n=6) ,when *p< 0.001 significant, **p< 0.01 highly significant.

CONCLUSION

From this study, we can state that the methanolic extract of leaves of *Coriandrum sativum* has beneficial effects on blood glucose levels . Based on the *in vivo* experimental study

and the active profile exposed through various biochemical parameters it can be concluded that the methanolic extract of leaves of *Coriandrum sativum* showed significant antidiabetic activity. Further investigations on the isolation and identification of bioactive components on the plant would help to ascertain its potency. Further pharmacological and biochemical investigation will clearly elucidate the mechanism of action and will be helpful in projecting this plant as an therapeutic target in diabetes research.

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