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INVESTIGATION OF ANTIDIABETIC ACTIVITY OF *LANTANA CAMARA* LINN. (VERBENACEAE) LEAVES

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ABSTRACT

The present investigation was carried out to evaluate the antidiabetic property of ethanol extract of *Lantana camara* Linn. (Verbenaceae) leaves (EELC) in alloxan induced diabetic rats. A single dose of alloxan monohydrate (150mg/kg, i.p) was used to induce diabetes mellitus. A comparison was made between the ethanol extract of *Lantana camara* Linn. and known antidiabetic drug glibenclamide. Dose selection of EELC was made on the basis of acute oral toxicity study according to the OECD guidelines. Oral administration of EELC at the doses of 250 and 500mg/kg were given to alloxan induced diabetic rats for 14 days. The Fasting Blood Glucose levels (FBG) levels were estimated on 0^{th}, 7^{th} and 14^{th} day. The blood was collected and serum was separated for the estimation of biochemical parameters. The EELC at 250 and 500mg/kg produces a dose-dependent fall in FBG levels. The extract also prevented body weight loss in diabetic rats. The results indicate that ethanol extract of *Lantana camara* Linn. leaves possess significant anti-diabetic activity.

Keywords: *Lantana camara* Linn., Antidiabetic activity, Medicinal plants, Alloxan induced diabetes.

INTRODUCTION

Diabetes mellitus is the most commonly occurring endocrine disorder which is characterized by hyperglycemia and disturbances in carbohydrate, protein and fat metabolism; and leads to an absolute or relative lack of hormone insulin. Apart from hyperglycemia, other factors including dislipidemia or hyperlipidemia are involved in the development of micro and macro vascular complications, which are the major causes of morbidity and death [1]. According to the World Health Organisation (WHO), the prevalence of diabetes is likely to increase 35% by 2025. Statistical projection about India suggests that the number of diabetics will rise from 15 million in 1995 to 57 million in the year 2025 [2]. The occurrences of many undesirable reactions and adverse effects with the synthetic drugs have led to continuous and effective search for alternative drugs. Many indigenous Indian medicinal plants have been reported by various researchers to have anti-diabetic potentials. Ethno-medicinal interventions about medicinal plants possessing beneficial effects on diabetes are reported in approximately 800 plants [3]. Hence it is prudent to investigate herbal medicines as an option for treatment of diabetes.

Lantana camara Linn. (Verbenaceae) or red sage is native to Asia, tropical America and occurs throughout India. It is a gregarious, erect or half-climbing, aromatic shrub. Leaves are ovate, cuneate, dentate, pointed at the tip and rounded at the base and toothed in the margins. Flowers are orange, yellow or pink coloured [4]. Traditional practitioners of Asia and South America have been used *Lantana* species including *Lantana camara*, for centuries to treat various human ailments such as dermatological and gastrointestinal diseases, tetanus, malaria, tumors, diabetes and related complications [5, 6]. Therefore considering both ethno-medicinal and pharmacological applications of the plant we attempt to investigate the antidiabetic activity of the ethanol extract of leaves of *Lantana camara* Linn. (EELC) in alloxan induced diabetic rats.

MATERIALS AND METHODS

Plant collection and Authentication

The leaves of *Lantana camara* Linn. were collected from the forest region of Anantharam, Bhongir, Nalgonda district, Andhra Pradesh, in the month of September 2011. Care was taken to select plant with healthy leaves. The plant was authenticated by Prof. K Madhava Chetty, Botanist, SV University, Tirupati, Andhra Pradesh. The voucher specimen of the plant was deposited in the college for further reference.

Extraction of plant material

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The leaves of *Lantana camara* Linn. were collected, cleaned, dried in shade and pulverized in a grinder-mixer to obtain a coarse powder. The powder was passed through sieve No. 40 and stored in air tight container. The powder was subjected to continuous hot extraction with ethanol by using Soxhalation for 48 hours. The extract was dried under reduced pressure using rotary flash evaporator. The percentage yield of ethanol extract of *Lantana camara* Linn. leaves was found to be 27.89% w/w.

Animals used

Male Wistar albino rats (150-200g) were obtained from Sainath Enterprises CPCSEA (769/CPCSEA/2010) approved breader, Sainath Nagar, Uppal, Hyderabad, Andhra Pradesh. The animals were maintained in a well-ventilated room with 12:12 hour light/dark cycle in polypropylene cages. The animals were fed with standard animal food and water was given *ad libitum*.

Acute toxicity study

The acute toxicity studies of the ethanol extracts of *Lantana camara* Linn. leaves were carried out as per OECD guideline no. 423 (Acute Toxic Class Method). It was observed that the test extract did not produced mortality and morbidity even at 2000mg/kg dose. Therefore 250 and 500mg/kg doses were selected for further study [7].

Induction of Diabetes Mellitus

The overnight fasted rats were injected with Alloxan monohydrate dissolved in normal saline at a dose of 150mg/kg, b.w, i.p. Then rats were treated with 20% glucose solution (20ml/kg, b.w, i.p), after 6h of administration of alloxan monohydrate. Later, 5% glucose solution was given orally to the rats for 24h, to prevent hypoglycaemia. This model has been used in earlier studies to induce diabetes in rats [8, 9]. Rats with blood glucose levels more than 250mg/dl were considered diabetic rats and found with permanent diabetes were used for the study.

Experimental design

Animals were divided into Five groups each consisting of six rats. Group-I; Served as Normal Control rats, received Normal Saline (0.9%w/v). Group-II; Served as Diabetic Control (Disease Control) rats, received Alloxan monohydrate (150mg/kg, b.w, i.p). Group-III; Served as diabetic rats, treated with standard drug Glibenclamide (5mg/kg, p.o). Group-IV and Group-V; Served as diabetic rats, treated orally with ethanol extract of *Lantana camara*. Linn. leaves (EELC) at the dose of 250 and 500mg/kg respectively, daily once, for 14 days.

Antidiabetic study and Estimation of biochemical parameters

The effect of EELC in diabetic rats were studied by estimation of fasting blood glucose (FBG) levels on 0^{th}, 7^{th} and 14^{th} day by using glucometer. The mean body weight was measured during treatment on weekly basis. Serum was analysed for estimation of biochemical parameters (TC, TG, HDL, LDL and VLDL), after 14 days of treatment.

Statistical analysis

The data was expressed as mean ± standard error mean (S.E.M) for six animals in each group. The Significance of differences among the group was assessed using one way and multiple way analysis of variance (ANOVA). The test followed by Tukey-Kramer multiple comparison test, the p values less than 0.05 were considered as significance.

RESULTS

Acute Toxicity Study

In acute toxicity study the EELC treated rats at a higher dose of 2000 mg/kg did not exhibit any toxicity signs, difference in behaviour and changes in body weight at any time of observation. There was no mortality in the above mentioned dose at the end of 14 days of observation.

Effect of EELC on mean body weight of diabetic rats

The mean body weight of control and experimental rats were observed on 0^{th}, 7^{th}, 14^{th} day of treatment. Induction of alloxan monohydrate results in the reduction of mean body weight, which was prevented by EELC 250mg/kg and 500mg/kg after 14 days in dose dependent manner. The changes in mean body weight of all groups were represented in Table.1.

Effect of EELC on Fasting Blood Glucose levels of diabetic rats

Blood glucose levels in normal and experimental rats were tested on 0^{th}, 7^{th} and 14^{th} day during treatment with EELC at doses of 250mg/kg and 500mg/kg, p.o, which produced a dose-dependent fall in fasting blood glucose level. At the end of the experiment (14^{th} day) FBG level were found to be 135.06±6.39mg/dl and 125.31±5.17mg/dl in rats treated with EELC at the dose of 250mg/kg and 500mg/kg respectively. The changes in FBG levels of all groups were represented in Table.2.

Effect of EELC on Lipid Profile of diabetic rats

The levels of serum lipid profile such as triglycerides (TG), high density lipoproteins (HDL), low density lipoproteins (LDL), very low density lipoproteins (VLDL) and total cholesterol (TC) of all groups are shown in Table. The levels of TG, LDL, VLDL and TC were significantly elevated as well as levels of HDL were significantly reduced in diabetic rats when compared to normal control rats. A significant percentage reduction of TG, LDL, TC and VLDL level and increase in HDL level was observed in rats treated with standard drug glibenclamide as well as rats treated with EELC at the doses of 250 and 500mg/kg in dose dependent manner. The changes in lipid profile of all groups were represented in Table.3.

Table 1. Effect of EELC on Mean Body Weight of diabetic rats

Groups (n=6)	Mean body weight (g)		
	0th Day	7th Day	14th Day
Group-I	189.27±2.29***	192.31±2.14***	196.15±2.23***
Group-II	187.21±2.17	180.27±2.23	170.51±4.65
Group-III	173.53±3.52	175.51±3.32***	180.12±2.91***
Group-IV	175.24±3.46	176.15±3.62***	179.24±3.13***
Group-V	180.62±4.72	182.42±4.44***	186.09±4.31***

Values are expressed as mean ± SEM sum of 6 rats in each group. *** p<0.001, Groups III, IV & V are compared with Group II (diabetic control rats).

Table 2. Effect of EELC on Fasting Blood Glucose Levels of diabetic rats

Groups (n=6)	Fasting Blood Glucose levels (mg/dl)		
	0th Day	7th Day	14th Day
Group-I	90.85±3.95***	91.28±4.16***	91.10±3.16***
Group-II	255.13±4.12	268.82±3.90	277.47±3.06
Group-III	256.91±5.05	186.32±5.32***	120.12±4.36***
Group-IV	260.13±4.14	210.51±2.27***	135.06±6.39***
Group-V	270.18±2.42	191.62±5.07***	125.31±5.17***

Values are expressed as mean ± SEM sum of 6 rats in each group. *** p<0.001, Groups III, IV & V are compared with Group II (diabetic control rats).

Table 3. Effect of EELC on Lipid profile of diabetic rats

Groups (n=6)	Biochemical Parameters (mg/dl)				
	TG	HDL	LDL	VLDL	TC
Group-I	72.25±1.32***	35.28±3.03***	32.81±3.16***	17.08±0.81***	81.61±3.21***
Group-II	132.51±1.73	19.19±1.14	75.07±4.92	32.40±5.01	138.08±.68
Group-III	78.89±1.61***	33.62±1.30***	33.84±0.26***	18.94±0.85***	83.92±0.42***
Group-IV	95.4±2.15***	31.61±0.32***	36.65±0.38***	21.09±0.98***	85.35±0.36***
Group-V	81.12±0.46***	32.04±0.04***	34.09±0.62***	19.41±1.38***	84.09±0.25***

Values are expressed as mean ± SEM sum of 6 rats in each group. *** p<0.001, Groups III, IV & V are compared with Group II (diabetic control rats).

DISCUSSION

Diabetes mellitus is not a single disease; it is rather a heterogeneous group of syndromes characterized by elevation of blood glucose levels caused by a relative or absolute deficiency of insulin. It is characterized by hyperglycemia, glycosuria, hyperlipidimia and sometimes ketonemia [10]. Alloxan, a β-cytotoxin, destroys β-cells of islets of Langerhans of pancreas which results in reduction of endogenous insulin secretion and leads to elevation of blood glucose levels [11]. Medicinal plants have been reported to possess anti-diabetic activity. *Lantana camara* Linn. leaves are gaining much importance in diabetic control as it has been used as a traditional medicine for diabetes. Since the phytochemical analysis has shown the presence of phytochemicals like flavonoids, terpenoids, glycosides, steroids, saponin and phenols. Several researchers reported that flavonoids, steroids, terpenoids and phenolic acids are known to be bioactive antidiabetic principles [12, 13]. Flavonoids are known to regenerate the damaged beta cells in the alloxan induced diabetic rats and acts as insulin secretagogues [14]. Saponin reduces the uptake of certain nutrients including glucose and cholesterol at the gut through intra-luminal physicochemical reaction [15].

The alloxan induced diabetic rats (Group III, IV and V) were treated with standard drug glibenclamide and ethanol extracts of *Lantana camara* Linn. at the doses of 250 and 500mg/kg body weight respectively for 14 days. The results of mean body weight, fasting blood glucose (FBG) levels and estimation of biochemical parameters of treated groups were compared with diabetic control rats (Group II). Glucose, insulin, lipid profiles, protein and antioxidants were restored to normal levels with the administration of the known drug glibenclamide and plant extracts *Lantana camara* Linn. (Verbenaceae).

CONCLUSION

It is concluded from this investigation, that the ethanol extract of *Lantana camara* Linn. (Verbenaceae) leaves possess significant anti-diabetic potential and support its traditional use to treat diabetes. The present study has also opened opportunities for further research, especially regarding development of potent formulation for diabetes mellitus from *Lantana camara* Linn. (Verbenaceae) leaves.

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