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EVALUATION OF HYPOGLYCEMIC AND ANTI HYPERLIPIDAMIC POTENTIALS OF EUPHORBIA LOPOGONA LINN. LEAVES ON ALLOXAN INDUCED DIABETIC AT MODEL

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Abstract:

The concerned study reveals the experimental investigation of the biological activity of *Euphorbia lopogona* (Family: Euphorbiaceae) used as a traditional antidiabetic and hypolipidemic agent in past and present culture. To study the effect of *Euphorbia lopogona* in both normal and alloxan induced diabetic rats. The aqueous leaf extract of *Euphorbia lopogona* at the dose of 400, 600 and 800 mg kg⁻¹ body weight was administered orally once a day to the groups for 30 days. The fasting blood glucose, cholesterol, HDL cholesterol and serum triglyceride content were estimated in both normal and alloxan induced diabetic rats. The fasting blood glucose, cholesterol and serum triglyceride content were found to be significantly reduced ($p < 0.05$) in treated rats whereas the extract also showed the potent elevation in the level of serum HDL cholesterol. The study reveals that *Euphorbia lopogona* has significant antidiabetic activity and a hypolipidemic activity in alloxan induced and normal fasting rats. The extract seems promising for the development of a phytomedicine for diabetes mellitus.

Key words

Antidiabetic Diabetes mellitus *Euphorbia lopogona* Hypolipidemic activity.

Introduction

Diabetes mellitus is syndrome, initially characterized by a loss of glucose homeostasis resulting from defects in insulin secretion, insulin action both resulting impaired metabolism of glucose and other energy-yielding fuels such as lipids and protein. Diabetes mellitus is a common disorder among the Indian population. It is estimated that diabetes would

affect approximately 57million people by the year 2025. Therapeutic options for diabetes are diet, exercise, oral hypoglycemic drugs and insulin therapy. Plant drugs are frequently considered to be less toxic and free from side effects than synthetic one. Although, there are numerous traditional medicinal Plants reported to have antidiabetic and hypoglycemic properties. A member of the milkweed family (Family: Asclepiadaceae) *Euphoria lopogona* is a woody plant found in tropical forests of India and Africa has been proven as ant diabetic drug. The medicinally active parts of the plant are the leaves and the roots although the exact mechanism is unknown. Besides impairing the ability to discriminate sweet taste increase enzyme activity responsible for the glucose uptake and utilization. It may stimulate pancreatic cell function, increase cell number and increase insulin release by increasing cell permeability to insulin. Drug interaction occurs from the additive effect when used concomitantly with hypolipidemic agent. Hence in the present study an attempt is made to elucidate the possible antidiabetic and hypolipidemic activity of *Euphoria lopogona* aqueous leaf extract on both normal and alloxan induced diabetic rats.

Methods and Materials

Animals

Male albino rats, weighing about 150–200 g obtained from the Mahaveer Enterprizes, Bagh Ambarpet, Hyderabad (CPCSEA registration no: 146/1999/cpcsea) and the animals were kept in the animal house of Sree College of Pharmacy, Nayakula gudem, kotha gudem Kammam A.P - 507020 at room temperature of 25 - 30°C and at 45 - 55% relative humidity for 12 hr, each of dark and light cycle. The animals were feed with rat pellets (Hindustan Lever Limited, Bangalore, India) and filtered water. Animal studies in the work have been strictly performed as per the Institutional Animal Ethical Committee (IAEC) constituted under the guidelines of Committee for the Purpose of Control and Supervision on experimental Animal (CPCSEA), Ministry of Environment, and Govt. of India.

Collections of plant materials

The leaves of *Euphoria lopogona* (ASF) collected from Kothagudem forest AndhraPradesh India between November and December; the plant was authenticated by the Professor R Venu Gopal, SR&BGNR Govt. Degree & PG College Kothagudem, Kammam Dts. A voucher specimen (SSR 2013/12/14) has been preserved in our laboratory. The plants were washed thoroughly in tap water, shade dried and powdered.

Determination of acute toxicity

Acute toxicity study was conducted for ethanolic extract of ASF by stair case method following OECD guidelines (K. Dash et al). There was no lethality up to a dose of 1000 mg/kg, p.o. Nearly one tenth of the maximum dose of the extract that is 400, 600 and 800mg/kg(p.o) was selected as the plant extract dose in all experiments

Preparation of Aqueous Extract:

One hundred grams of dry fine powder was suspended in 250 ml of water for two hours and then boiled at 60°C to 65°C for 30 minutes (since boiled decoction of the leaf of this plant has been used as remedy for diabetes). The collected extract was pooled and passed through a fine cotton cloth. The filtrate upon evaluation at 40 c yield 20% semi solid extract

Drugs and Chemicals:

Alloxan monohydrate was purchased from BDH Chemicals, Poole, England. All other chemicals used were of analytical grade.

Drug Administration:

After seven days of alloxan induction, the aqueous leaf extract was administered orally through intragastric tube at the following doses of 400, 600 and 800 mg kg body weight.

Experimental Induction of Diabetes:

The rats were injected intraperitoneally with alloxan monohydrate dissolved in sterile normal saline at a dose of 150 mg kg body weight. Blood samples were collected before the administration of alloxan and after 5 days of alloxan administration. Diabetic state was confirmed when the blood sugar level was above 200 mg/dl. The rats with moderate diabetes and hypolipidemia were used for the experiment.

Animal Allotment:

After the induction of diabetes the rats were divided in to a five different groups of six rats each.

Group I: Control rats received normal saline and fed on normal diet.

Group II: Diabetic control.

Group III: Diabetic rats received *Euphoria lopogona* leaf extract (400 mg kg 1 body weight) daily using an intragastric tube for 30 days.

Group IV: Diabetic rats given *Euphoria lopogona* leaf extract (600 mg kg⁻¹ body weight) daily using an intragastric tube for 30 days.

Group V: Diabetic rats received *Euphoria lopogona* leaf extract (800 mg kg⁻¹ body weight) daily using an intragastric tube for 30 days.

At the end of 0, 10, 20 and 30 day blood was collected in tubes containing potassium oxalate and sodium fluoride solution for the estimation of glucose and lipid profile.

Biochemical Analysis

Estimation of Blood Glucose: Blood glucose was determined by the O-toluidine method.

Estimation of Total Cholesterol (TC): Total cholesterol level was determined by the commercially available reagent kit (Erba Mannheim, Transasia biomed, Daman, India). It is based on (CHD_PAP) enzymatic methods.

Estimation of HDL-cholesterol: HDL-cholesterol level was determined by commercially available reagent kit on phosphotungstate method

Estimation of Triglyceride (TG)

Triglyceride level was estimated by commercially available kit. Its working is based on enzymetic colorimetric method. This reagent kit was made for in vitro quantitative determination of triglycerides in serum or plasma. Our study was carried out by the serum.

Statistical Analysis

Data were expressed as mean \pm SE. statistical analysis one was done using one –way analysis of variance (ANOVA) followed by Tukey's multiple comparison. Values were considered statistically significance when at $p < 0.05$.

Results

The various doses of aqueous extract of *Euphoria lopogona* were given to the diabetic rats once a day and changes in fasting blood glucose, total cholesterol, cholesterol and triglyceride were measured on day 10, 20 and 30 from the day of first dose of experiment. An effective reduction in fasting blood glucose level was observed on above mentioned time. Reduction was examined at all doses of given plant extracts but highest concentration (800 mg/ kg/ body weight) was resulted maximum on all observed days. Although, a drastic reduction of fasting blood glucose was found to be at 400 mg / kg / body weight compared with other doses (Table 1). Diabetic control showed negligible change whereas

maximum percentage reduction of 61, 66 and 69% were recorded on 30th day in group fed aqueous leaf extract at 400, 600 and 800 mg kg⁻¹ body weight respectively (Fig. 1).

The change in the cholesterol, HDL-cholesterol and triglyceride level was measured and observed on potent reduction in serum cholesterol, triglycerides and effective elevation in HDL-cholesterol level over diabetic control when the rats fed aqueous leaf extract. The level of serum cholesterol was lower in normal rats that were not treated with alloxan and elevation were found in diabetic control (Table 2) whereas maximum percentage reduction 19, 44 and 46 % were seen on 10 , 20 and 30 day during the course of 800 mg kg⁻¹ body weight treatment (Fig. 2). In respect to HDL-cholesterol, it showed decrement in normal rats (Table 3) but maximum elevation of 20, 29 and 30% were recorded on 10 , 20 and 30 day due to 800 mg kg⁻¹ body weight concentration of aqueous leaf extract(Fig. 3). However, similar trends of HDL-cholesterol elevation were observed at all doses of treatments with given time periods. Rats fed aqueous leaf extract were showed inhibition in serum triglyceride content (Table 4) which was recorded in percentage 44, 47 and 50%

Table 1: Change in fasting blood glucose levels of control and experimental animals.

S No	Group	Fasting blood glucose mg/dL			
		0 th day	10 th day	20 th day	30 th day
1.	Normal	85+1.6	87.6+2.4	87.3+2.6	89.3+2.4
2.	Diabetic (control)	299+3.4	311+2.3	310.2+2.4	301+2.6
3.	A extract (400mg/kg)	284+2.3	123.6+2.8	119+3.1	110.5+2.3
4.	A extract (600mg/kg)	291.6+2.1	112.6+2.0	106.2+2.7	100+2.8
5.	A extract (800mg/kg)	289.6+2.6	98.1+2.9	95.7+2.8	90+2.5

Table 2: Change in total cholesterol levels of control and experimental animals.

S No	Group	Total cholesterol (mg/dl)			
		0 th day	10 th day	20 th day	30 th day
1.	Normal	129±1.2	132.4±3.2	134.2±2.7	134±2.9
2.	Diabetic (control)	260.3±2.5	254.7±2.4	268.5±2.5	275±2.2
3.	A extract (400mg/kg)	258.6±3.2	211.1±2.3	179.4±2.9	162±1.5
4.	A extract (600mg/kg)	247.2±2.3	205±2.1	168.2±2.2	152.2±3.1
5.	A extract (800mg/kg)	250±2.4	203±2.9	149.6±4.9	142±2.4

Table 3: Changes in HDL-cholesterol content of control and experimental animals.

S No	Group	Serum HDL level (mg/dL)			
		0 th day	10 th day	20 th day	30 th day
1.	Normal	44.2±1.1	43±2.7	41.5±2.8	40.5±2.2
2.	Diabetic (control)	49.6±1.8	41.2±3.1	40.7±2.7	38.5±2.2
3.	A extract (400mg/kg)	48.2±2.7	44.3±2.8	50.2±2.6	55.5±1.6
4.	A extract (600mg/kg)	52.3±2.6	55.1±2.9	58.7±2.7	61.7±2.2
5.	A extract (800mg/kg)	56.3±2.0	59.3±2.2	63±2.9	64.2±1.9

Table 4: Changes in serum triglyceride (TG) content of control and experimental animals.

S No	Group	Serum triglyceride levels (mg/dL)			
		0 th day	10 th day	20 th day	30 th day
1.	Normal	80.6±1.6	81.5±2.6	78±2.7	79.7±2.5
2.	Diabetic (control)	187±2.6	192.5±2.5	186.7±1.4	179.5±2.5
3.	A extract (400mg/kg)	184.3±2.3	169.7±2.7	148±3.0	134±2.2
4.	A extract (600mg/kg)	176.6±2.6	154±2.1	132.6±2.5	128.2±2.1
5.	A extract (800mg/kg)	169.5±2.9	150.5±2.5	119.7±2.9	105.4±1.3

On 10th, 20th and 30th day but remarkable reduction of serum triglyceride was noted on feeding at 400 mg kg⁻¹ body weight extract at all days of observations (Fig. 4).

Discussion

Alloxan, a cytotoxin, induces “chemical diabetes” in a wide variety of animal species by damaging the insulin secreting pancreatic β -cells, resulting in a decrease in endogenous insulin release, which paves the ways for the decreased utilization of glucose by the tissue. In our study, we have observed that *Euphoria lopogona* decreases fasting blood glucose in alloxan diabetic rats that may be due to increase the activity of enzymes responsible for utilization of glucose by insulin-dependent pathway or regenerate β -cells in pancreatic islets. Like the plant extract, glibenclamide also produced significant reduction in blood glucose levels of alloxan diabetic rats, the present findings appear to be in consonance with the earlier suggestion. In this study, the feeding of *Euphoria lopogona* leaf extract resulted in

significantly decreased total cholesterol and serum triglycerides and significantly increased HDL- cholesterol level; these findings are correlated with the experiment. Ingestion of *Euphoria lopogona* produced a significant lowering of cholesterol in a hypertension model. Insulin is potent inhibitor of lipolysis since it inhibits the activity of the hormones sensitive lipases in adipose tissue and suppresses the release of triglycerides. The increase in HDL-cholesterol levels may be beneficial owing to the negative correlation between HDL-cholesterol levels and cardiovascular diseases. This could be due to the presence of other hypolipidemic agents such as sitosterol in the aqueous leaf extract.

Conclusion

Diabetes mellitus is a well known clinical entity with various late complications like retinopathy, neuropathy, nephropathy etc. *Euphoria lopogona* has significant antidiabetic as well as hypolipidemic activity so that it can be used as an adjuvant along with allopathic treatment of medicine to treat diabetes as well as to delay the late complications of diabetes. Further study is underway in our laboratory to isolate the active principle and to study the mechanism of its action

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