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HYPOGLYCEMIC AND ANTI-DIABETIC ACTIVITY OF METHANOLIC EXTRACT OF LEAVES OF *STRIGA GESNERIODES* ON ALLOXAN INDUCED MODEL IN RATS

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ABSTRACT

Objective: The present investigation was aimed to study the antidiabetic potential of the methanolic extract of leaves of *Striga gesnerioides* in alloxan induced diabetic rats.

Materials and methods: Acute toxicity was studied in rats at 3000mg/kg dose of extract and diabetes was induced in rats by administration of alloxan (150mg/kg i.p). After 7 days of blood glucose stabilization, diabetic rats received extract and glibenclamide up to 21 days. The blood samples were collected on day 21 to estimate body weight and blood glucose levels.

Results: In acute toxicity study the extract did not show any toxicity or death up to 3000mg/kg. Therefore to assess antidiabetic activity nearly 1/5th and 1/10th of extracts were selected. Administration of 500mg/kg and 300mg/kg dose in diabetic rats showed significant reduction in blood glucose level and increase in body weight than diabetic control rats. The methanolic extract also showed improvement in regeneration of β -cells of pancreas in diabetic rats.

INTRODUCTION

Diabetes mellitus is a term employed to describe a metabolic disorder characterized by persistent hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action or both. It is considered as one of the five leading causes of death in the world ^[1]. In modern medicine there is no effective therapy to cure diabetes mellitus ^[2]. There is increasing demand by patients to use natural products with antidiabetic activity due to side effects associated with the use of insulin and oral hypoglycaemic agents ^[3]. There are numerous traditional medicinal plants reported to have hypoglycaemic properties but many of these are less effective in lowering glucose levels in severe diabetes.

MATERIALS AND METHODS

Plant material: The basic plant material of *Striga gesnerioides* leaves was used for investigation was obtained from srivenkateshwara university, Tirupathi. The plant can be identified, authenticated by Dr. Madhavachetty, SV university, Tirupathi.

Preparation of extract: The leaves of plants were collected and shadow dried. The shade dried leaves were subjected to pulverization to get coarse powder. The coarsely powdered leaves (1kg) of *Striga gesnerioides* was used for extraction with methanol in soxhlet apparatus. The extract was evaporated to dryness under vacuum and dried in desiccator.

Animals: Wistar albino rats (8-10 weeks) of both sexes were obtained from animal house of NIN, Hyderabad. Before and during experiment, rats were fed with standard diet after randomization the rats were acclimatized for a period of 7 days under standard environmental condition of temp ($22^{\circ}\text{C}\pm 2^{\circ}\text{C}$), relative humidity ($45\% \pm 5\%$) and dark/ light cycle of 12:12 hrs

Oral glucose tolerance test: Rats were divided into six groups containing six animals each. All the animals were fasted before treatment. Group I treated as vehicle which received 5% Tween 80 p.o, Group II received glucose only, Group III received 300mg/kg extract, Group IV received 500mg/kg extract, Group V received only 300mg/kg extract and Group VI received only 500mg/kg extract. Group III and Group IV were loaded with glucose (4g/kg p.o) 30 min after drug administration. Blood samples were collected from puncturing the retroorbital sinus just prior drug administration and 30, 60, 90 and 120 mins after loading glucose. Serum glucose level was measured immediately by using glucose estimation kit.

Acute oral toxicity studies: *Striga gesnerioides* at dose range of 100mg -200mg/kg were administered orally to different groups of rats comprised of ten rats in each group. Mortality was observed after 72 hours. Acute toxicity was determined according to the method of Litchfield and wilcoxon^[4].

Induction of diabetes in experimental animals: Rats were made diabetic by single intraperitoneal injection of alloxan monohydrate (150mg/kg). Alloxan was first weighed individually for each animal according to body weight and then solubilised with 0.2ml saline just prior to injection. Two days after alloxan injection, rats with plasma glucose levels of >140 mg/dl were included in the study.

GROUPS	Treatment	Blood glucose levels in mg/dl			
		0 day	7th day	14th day	21st day
CONTROL	Normal Saline	99.28±2.66	97.28±2.11	98.54±1.03	97.4±0.65
DIABETIC CONTROL	Alloxan 150mg/Kg I.P	272.7±7.8	288±4.72	291.25±3.70	308.26±4.35
STANDARD	Alloxan 150mg/Kg I.P + Glibenclamide 5mg/Kg PO	270.43±5.90	108.64±2.92**	97.2±1.2**	88.64±2.71*
MESG 300MG/KG	Alloxan 150mg/Kg +MESG 300mg/Kg Po	276.28±5.32	204.57±4.39	184.8±3.71	164.66±4.33
MESG 500MG/KG	Alloxan 150mg/Kg +MESG 500mg/Kg PO	274.21±4.91	154.23±3.72*	125.83±4.6*	105.83±2.85**

Experimental design: Five groups of rats, six in each received the following treatment schedule.

Group-I: Normal control (saline)

Group-II: Alloxan treated control (150mg/kg i.p)

Group-III: Alloxan (150mg/kg i.p) + MESG (300mg/kg p.o)

Group-IV: Alloxan (150mg/kg i.p) + MESG (500mg/kg p.o)

Group-V: Alloxan (150mg/kg i.p) + standard drug glibenclamide (5mg/kg p.o)

Plant extracts, standard drug glibenclamide (5mg/kg) and saline were administered with the help of feeding cannula. Group-I serves as Normal control which received saline for 21 days. Group-II to V are diabetic control rats. Group-III to V (which previously received alloxan) are given a fixed dose of extract (300mg/kg, 500mg/kg p.o) and standard drug glibenclamide (5mg/kg) for 21 days.

Collection of blood samples and blood glucose determination: Blood samples were drawn from rats by retro-orbital puncture. Fasting blood glucose estimation and body weight measurement were done on day 0,7,14 and 21st of study. Blood glucose estimation can be done by one touch glucometer by using glucose test strips.

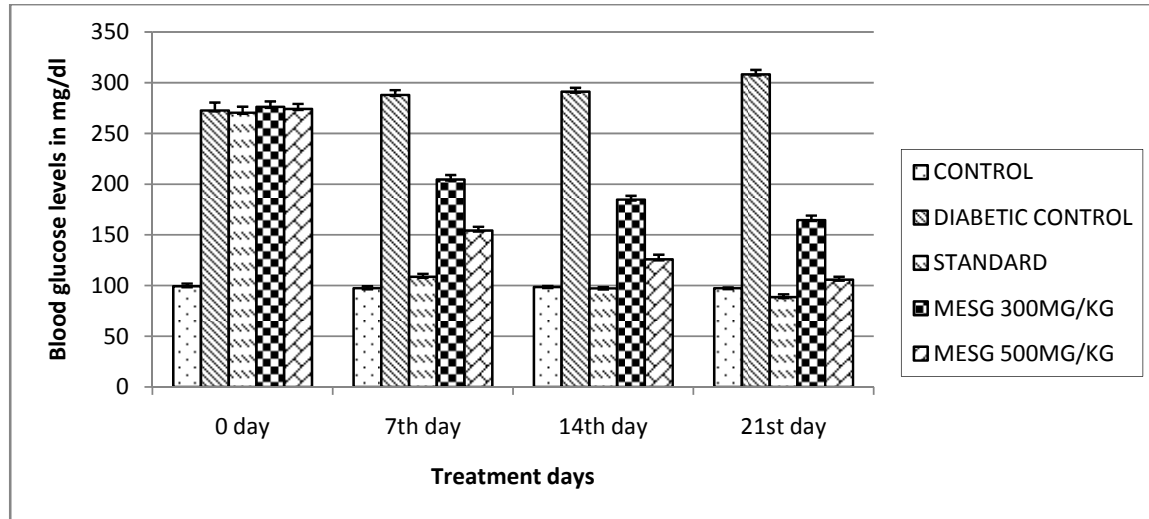
One day 21st, blood was collected from retro-orbital plexus under mild ether anaesthesia and blood sugar was estimated.

Statistical analysis: All the values were expressed as mean \pm SEM (standard error mean) and analysed for one way ANOVA and Dunnet's t-test. Difference between groups were considered significant at $P < 0.01$ levels.

RESULTS

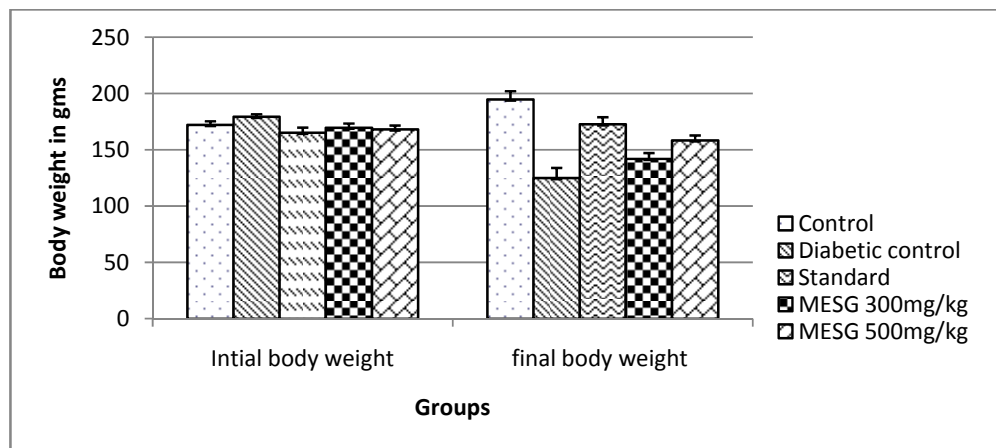
Blood glucose estimation:

Each value is the mean \pm SEM for 6 rats, * $P < 0.5$, ** $P < 0.01$, *** $P < 0.001$. Compared with control, data were analysed by using one-way ANOVA followed by Dunnet's test.



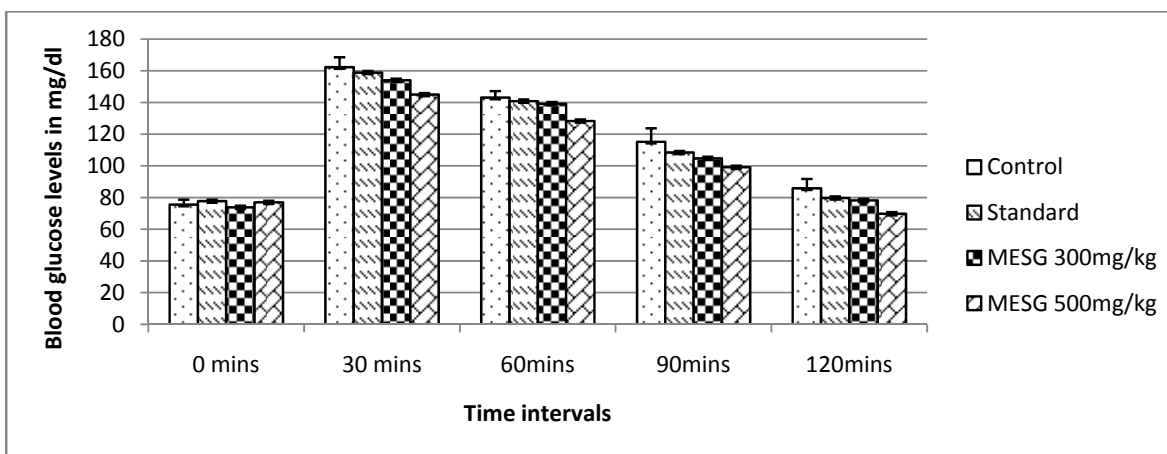
Body weight measurement:

GROUPS	Initial body weight	Final body weight
Control	172.2 \pm 3.20	194.75 \pm 7.37
Diabetic control	179.7 \pm 2.22	125 \pm 9.01
Standard	165.20 \pm 4.60	172.75 \pm 6.22
MESG 300mg/kg	169.70 \pm 3.71	142.0 \pm 5.17
MESG 500mg/kg	168.20 \pm 3.40	158.5 \pm 4.34



Oral glucose tolerance test:

Groups	Treatment	0 mins	30 mins	60mins	90mins	120mins
Control	Glucose 4g/kg	75.62±3.10	162.34±6.21	143.15±4.07	115.24±8.54	85.87±5.94
Standard	Glucose 4g/kg + glibenclamide 5mg/kg	77.78±4.53	158.91±6.02	140.92±6.18	108.47±8.76	79.77±5.68
MESG 300mg/kg	Glucose 4g/kg + MESG 300mg/kg	73.89±5.94	154.03±8.76	139.28±9.23	104.78±10.26	78.24±8.54
MESG 500mg/kg	Glucose 4g/kg + MESG 500mg/kg	77.02±5.05	145.01±6.10	128.34±9.16	99.14±7.14	69.84±7.68

**DISCUSSION**^[5-8]

Diabetes Mellitus is a major health problem worldwide but its therapeutic management still suffers from major Limitations. Global estimates suggests that 3/4th of world population cannot afford the products of allopathic medicine and thus, have to rely upon the use of traditional medicines with are largely from plants. Natural remedies from medicinal plants are considered to be effective and safe alternative treatment for diabetes mellitus. The present paper discussed about the hypoglycemic and ant diabetic activity of *Striga gesnerioides* leaf in experimentally induced diabetes in rats. The oral glucose tolerance test is a well accepted and frequently used assay to screen hypoglycemic activity. MESG might hence glucose utilization since it significantly reduces blood glucose in normal rats fed with glucose. From the data obtained with oral glucose tolerance test, it is evident that blood glucose levels reached a peak and returned to initial normal levels after 120 min in both normal and MESG 300mg/kg and 500mg/kg treated rats. MESG treatment effectively prevented the rise in diabetic rats without causing hypoglycemic state. This might be due to inhibition of intestinal absorption of glucose or due to restoration of delayed insulin response.

Alloxan induces chemical diabetes in a wide variety of animal species by damaging the pancreatic beta cells which secrete insulin. Alloxan induces hyperglycemia by specific impact on pancreatic beta cells, its cytotoxicity is through the production of free radicals. From the results, MESG at 500mg/kg showed significant antidiabetic activity upon repeated administration when compared with MESG at 300mg/kg. MESG 500mg/kg is more effective and shows similar curative effect as standard that is glibenclamide at 5mg/kg. The antidiabetic activity may be due to increased peripheral consumption of glucose or due to increased release of insulin from still surviving beta cells or due to make insulin free from its bound state or due to decreased absorption of glucose from intestine. One of the major complications of type II diabetes is weight loss. It rises due to the impairment in insulin action in the conversion of glucose to glycogen and catabolism of fats, inhibition lipolysis due to its unavailability because of destruction of beta cells of pancreas. Due to these there will be weight loss and death. Treatment with MESG has substantially prevented the weight loss and mortality produced by alloxan.

The results of blood glucose levels, glucose tolerance and body weight are in correlation with each other and indicate that MESG can be beneficial in reducing the effect of alloxan induced diabetes.

CONCLUSION

The present study justifies the traditional use of *Striga gesnerioides* leaf in the treatment of diabetes and has opened avenue for further research especially with reference to the development of potent phytomedicine for diabetes mellitus from *Striga gesnerioides*. Further phytochemical and pharmacological investigations are in progress to understand the exact mechanism of action of this leaf extract.

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