HYPOGLYCEMIC EFFECT OF *PHOEBE LANCEOLATA* ON ALLOXAN-INDUCED DIABETIC MICE

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Summary

The present study was based on the antidiabetic effect of ethanolic extract of *Phoebe lanceolata* stem bark. Swiss albino mice were administered ethanolic *P. lanceolata* stem bark extract orally at doses of 100, 200 and 500 mg/kg, *p.o.* Alloxan (60 mg/kg, *i.v.*) was used to increase the blood glucose level in experimental mice. From 1st to 18th h significant hypoglycemic effect was observed with maximum effect at 18th h. Glibenclamide, an oral hypoglycemic agent was used as positive control.

Keywords: *Phoebe lanceolata*, Lauraceae, antidiabetic activity, alloxan and albino mice

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Introduction

The herbal medicines have recently gained popularity and scientific interest. Researchers have been interested in biologically active compounds isolated from plants species for the treatment of metabolic disorders like diabetes. Diabetes mellitus is one of the chronic, world wide heterogeneous, lives threatening disease. The prevalence of it will be 5.4% by the year 2025, with the global diabetic population reaching to 300 million. Among all the WHO regions, South East Asian region are highest affected with maximum global burden of the disease and by year 2025 there will be nearly 80 million diabetic in the region (1).

There are many plants present in nature possess marked hypoglycemic activity. Although, the extracts obtained from these plants have a significant activity to treat the disease, however the potency of these extracts can be increased either by the purification of crude extract or by the isolation of individual constituent responsible for such activities.

P. lanceolata (Lauraceae) is well reputed in traditional medicine of India (2). The berries from the plant are used in wounds and sores. The paste obtained from the roots bearing aromatic smell is used in fractured bones by natives. Recently nordelporphine alkaloid (3) and oxoaporphine alkaloids (4), together with known β-sitosterol and its monoglucoside were isolated from stem bark of the plant. Herein, we report the hypoglycemic activity of ethanolic extract from stem bark against alloxan-induced diabetic mice.

Material and methods

Plant material

Stem bark of *P. lanceolata* was collected from Kartikswami temple, Chamoli, India during July 2006 and identified from Taxonomical Laboratory, Department of Botany, H.N.B. Garhwal University, Srinagar. A voucher specimen (GUH-17598) of the plant was deposited in the departmental herbarium.

Preparation of extract

Coarsely powdered stem bark was extracted exhaustively with 95% ethanol at 50 $^{\circ}$C for 15 h. Extract was concentrated under reduced pressure and administered for antidiabetic activity.

Preparation of doses

The oral doses of *Phoebe lanceolata* (PL) at 100, 200 and 500 mg/kg, *p.o.*, body weight were prepared in distilled water for determination of hypoglycemic effect whereas the oral doses of 200, 500 and 1000 mg/kg, *p.o.*, were prepared for LD_{50} experiments. Glibenclamide (as standard) 5 mg/kg, *p.o.* was prepared with distilled water.

Study of test drug and positive control on experimental animals

Swiss albino mice of either sex (35-50 g body weight) were employed for present study. These animals were deprived to food for 16 h but allowed free access to water. They were housed in the departmental animal house and exposed to normal light. Experiments were performed according to the guidelines for the care and use of laboratory animals, from the CPCSEA, Ministry of Environment and Forest, Govt. of India (Reg. No.-107/1999/ CPCSEA). After deprived to food for 16 h, mice were divided into six groups (six animals each), (I-VI), namely normal control, diabetic control, diabetes + PL-100, diabetes + PL-200, diabetes + PL-500 mg/kg and positive control. Induction of diabetes was performed using a modification in the method described by Shan et al. (5). The diabetes was produced by an injection of alloxan (60 mg/kg, dissolved in saline) in the tail vein of mice. The diabetic state was assessed by blood glucose levels 36 h later of alloxan administration, the mice having blood glucose more than 150 mg/dL were only selected for the study. Animals which presented glucose levels lower than 150 mg/dL were rejected. The group of normal control (I) was not administered by alloxan and only received distilled water. Rest of the groups (II-VI) received alloxan and 36 h later were treated with distilled water (diabetic control), group III-V with 100, 200 and 500 mg/kg, *p.o.* respectively of *P. lanceolata* (PL) and group VI was treated with glibenclamide 5 mg/kg, *p.o.* as standard.

Blood samples of normal and alloxan induced diabetic mice were collected at 0, 1, 3, 6, 18 and 24 h during the treatment. In each case, 10 μL of serum sample was collected and estimated for glucose by GOD-POD method (6).

LD_{50} Experiment

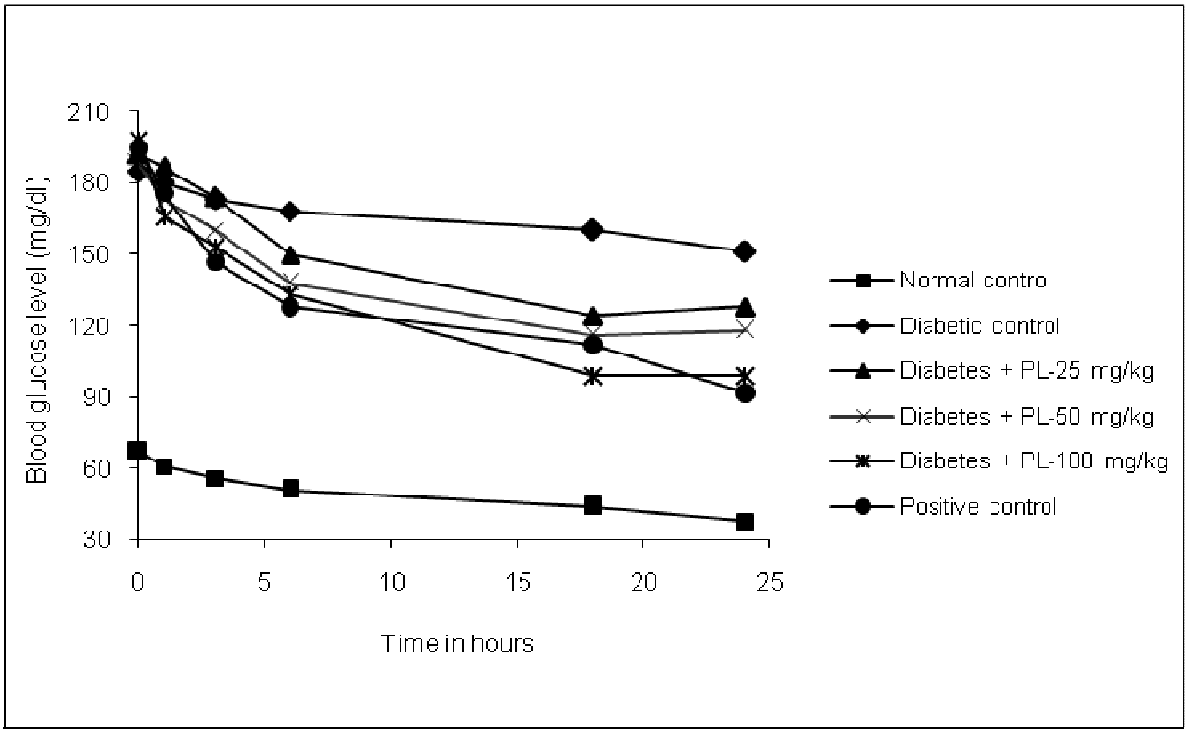
The mice were administered PL, orally at doses of 200, 500 and 1000 mg/kg, *p.o.*, body weight and observed continuous for 3 days intermittently up to 21 days for any gross behavioral changes and deaths.

Data and statistical analysis

Results are expressed as the mean ± S.E.M. of 6 independent experiments. The data were analyzed for statistical significance by one-way ANOVA test; P values < 0.05 were considered to be significant.

Results

The treatment of alloxan induced diabetic mice for 24 h with ethanolic extract of PL (100, 200 and 500 mg/kg) and glibenclamide (5 mg/kg), causes a significant reduction in blood glucose level as compared to diabetic control (group II). The normal control (group I) reduced the blood glucose by 28.36% whereas diabetic control reduced the sugar level by 18.38%. The dose of 100, 200 and 500 mg/kg *p.o.*, produced the hypoglycemic effect by 33.33, 37.23 and 50.00% respectively whereas the glibenclamide showed this effect by 52.82% upto 24 h. It is important to note that the hypoglycemic effect of 500 mg/kg (50.00%) of PL extract was found more significant as compared to positive control (42.56%) upto 18 h and beyond this limit the hypoglycemic effect was abolished for each dose of PL extract (Fig. 1).



Abr: PL- *Phoebe lanceolata*, Values are mean ± S.E.M. for six animals; positive control= glibenclamide

Fig.1. Effect of oral administration of different doses of *P. lanceolata* extract in the blood glucose level

Discussion

The present study showed that ethanolic extract of PL stem bark at a dose of 500 mg/kg, *p.o*., produced significant hypoglycemic effect in diabetic mice by 50% as compared to positive control, after 18 h of treatment. Hence the PL extracts may be considered to have good hypoglycemic principles without causing any side effect like insulin and other synthetic drugs. The phytochemical analysis (3) (4) of stem bark of PL extract revealed the presence of β-sitosterol; β-sitosterol-β-D-glucopyranoside, nordelporphine, laurodionine and N-6/C-7 oxalyl-fused 1,2,9,10-tetramethoxy 6a,7-didehydroaporphine. Since steroids and alkaloids are the major constituents of the extract, so these constituents could be responsible for hypoglycemic activity. Alloxan produced significant increase in blood glucose level by damaging pancreatic β-cells, resulting decrease in endogenous insulin secretion, which decreases the utilization of glucose by the tissues and thus used as effective diabetes-induction agent (7) for present study.

Conclusions

From the present study we may conclude that PL extract, in totality, was effective in reducing the blood glucose level in dose dependent manner under our experiment conditions and the extract of the test drug was found to be safe for further biological studies as no behavioral changes and lethality were observed upto 1000 mg/kg, *p.o*. in mice, after 21 days of the experiment. This extract is having long duration glucose lowering action because maximum effect was observed upto 18 h. Further investigations should be carried out on the purification and identification of the antidiabetic components of PL extract and to elucidate the mechanism of hypoglycemic effect of the extract. The extract showed significant hypoglycemic activity without any side effect and can be a source of new herbal drug in pharmaceutical industry as such or investigating the bio-active constituents from the extract for improving the potency.

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