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Hypoglycemic Activity of *Polygala erioptera* (Whole Plant) in Normal and Alloxan Induced Diabetic Rats

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Investigations were carried out to find out the hypoglycemic activity of alcoholic extract of *Polygala erioptera* Linn, in normal and diabetic albino rats and to evaluate its probable mechanism of hypoglycemic activity if any. Oral and intraperitoneal administration of the plant produced significant hypoglycemic effect in normal as well as hyperglycemic rats. It is suggested that the hypoglycemic activity of this plant may be mediated through enhancement of peripheral metabolism of glucose and increase in insulin release.

Key Words: *Polygala erioptera*, Diabetes mellitus.

INTRODUCTION

Diabetes mellitus is an endocrine disorder characterized by hyperglycemia effecting nearly 10 % of the population all over the world. Insulin and oral hypoglycemeic agents like sulphonylureas and biguanides are still the major players in the management of the disease. However, complete cure of the disease has been eluding physicians for centuries and the quest for the development of more effective antidiabetic agents is pursued relentlessly. Many herbal products, including several metals and minerals have been described for the cure of diabetes mellitus in ancient literature. Herbal preparations alone or in combination with oral hypoglycemic agents sometimes produce a good therapeutic response in some resistant cases where modern medicines alone fail. 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 hypoglycemic agents. The World Health Organization has also recommended the evaluation of the effectiveness of plants in condition where there is a lack of safe made drugs.

Currently available treatment for this disorder is far from satisfactory and expensive. *Polygala erioptera* Linn. (Family: Polygalaceae) is a small tree variety found throughout India including the Telangana region. It is commonly called Nela Janumu in Telugu and Surjavarta in Sanskrit[1,2]. It is

widely used for healing of wounds, effecive against chronic white discharge (leucoria), antibacterial and antifungal[3,4]. It is found to be muscarinic effect.

The preliminary phytochemical studies reveal the presence of flavanoid glycosides and flavones, flavanoids, lignans, fatty acids. The focus of the present study is to evaluate alcoholic extract of *Polygala erioptera* whole plant material at various doses in normal and alloxan induced diabetic rats. However, no scientific data are available regarding the effect of *Polygala erioptera* on blood glucose levels. The present study is undertaken to explore the effect of *Polygala erioptera* whole plant extract on the blood glucose level of experimental animals and to determine the probable mechanism of action. The effect of the alcoholic extract of *Polygala erioptera* on fasting blood sugar level has been evaluated as compared to the standard drug glibenclamide, both in normal and diabetic albino rats. The effects of *Polygala erioptera* extract on glucose uptake by rat hemi-diaphragm and the glycogen content of the liver, skeletal muscle and cardiac muscle are evaluated to study its probable mechanism of action as a hypoglycemic agent.

EXPERIMENTAL

Polygala erioptera Linn. whole plant material was collected during rainy season in the month of August freshly in and around The Kakatiya University, Warangal, South India. The botanist Dr. V.S. Raju, Department of Botany, Kakatiya University, Warangal, identified the plant.

Alcoholic extraction: Alcoholic extract was prepared from a powder of the whole plant material of *Polygala erioptera* prepared in electric grinder. The 500 g powder was extracted with alcohol (95 % v/v) in soxhlate apparatus. The extract was evaporated to dryness under vacuum and dried in vacuum desiccator (15.5 % w/w).

Animals and experimental set-up: Colony bred, healthy male Wistar albino rats (NIN strain) of either sex weighing 100-200 g were taken for the study. The animals were fed on standard laboratory diet with water *ad libitum* and housed at room temperature. The rats were kept fasting overnight with free access to water during the experiment in the same ambience. The animals were divided into three groups of six animals each. 1 mL of blood was taken from the orbital sinus of each rat with the help of a capillary tube for the estimation of blood sugar. The Institutional Ethics Committee approved all experimental protocols.

Hypoglycaemic effect in normal rats: Groups of eight rats each (fasted for 18 h) received 10 mL/kg of the infusion, intragastrically (p.o.) or intraperitoneally (i.p.). Blood samples were drawn by puncture from the tail immediately before administration and after administration in the time intervals of 20, 60, 120, 240 and 360 min later. Control group received an

equal volume (10 mL/kg) of normal saline, glibenclamide (0.13 mg/kg) and metformin (11.3 mg/kg), calculated on the basis of the daily doses (5 and 850 mg, respectively) for a man weighing 75 kg were used as refer ence drugs[5].

Hypoglycaemic effect on alloxan-diabetic rats: Chronically hyperglycaemic rats were obtained by i.p. injection of 150 mg/kg of alloxan dissolved in distilled water[6]. After 8 h administration, the hyperglycaemic rats were selected (plasma glucose level 2-2.8 g/L) and used in the experiments. The same experimental protocol described above was then adopted.

Glucose tolerance test (GTT) in rats: A polyethylene cannula was injected into the jugular vein under ethyl carbamate anaesthesia. Another catheter was injected into right carotid. All rats received orally 10 mL/kg of 25 % glucose solution. One group of animals received the plant infusion (10 mL/kg) through the venous catheter, while the control group received normal saline. Blood samples (0.2 mL) were taken from the carotid catheter at time intervals of 5, 10, 20, 30, 40, 50 and 60 min after injection. The coefficient of glucose assimilation (K_G) was determined with the formula.

$$K_G = (\log C - \log C/2)\ T_{½} = 0.639/T_{½}$$

where: C = glycaemia (g/L); $T_{½}$: Time for the blood glucose concentration C/2.

Statistical analysis: Results are reported as mean ± SEM statistical analysis was carried out using analysis of variance (Anova). The difference of the means was calculated using Newman-Keuls test. P values of 0.05 or less were taken as significant.

RESULTS AND DISCUSSION

The infusion of *Polygala erioptera* exhibited a remarkable hypoglycemic action 20 min after oral and i.p. administration to normal rats (Table-1). Blood glucose level reached a mean value of 0.59 and 0.68 g/L, respectively compared to 1.02 g/L obtained in the control group. The lowest hypoglycemic effect was observed 2 h after treatment. After 4 h administration, the blood glucose level rose to reach the initial glycemia values for orally treated animals, while i.p. administration still showed hypoglycemic effect even after 6 h. *Polygala erioptera* hypoglycaemic effect was comparable and sometimes higher than that obtained with 0.13 mg/kg of glibenclamide or 11.3 mg/kg of metformin.

After i.p. administration, the variation in insulin plasma levels showed an opposite trend to that of glucose (Table-2). The increase became significant after 1 h of administration and persisted for at least 6 h. Plasma insulin reached a maximum level (121.42 µIU/mL) 4 h after i.p. administration.

TABLE-1
EFFECT OF *P. erioptera* ON PLASMA GLUCOSE LEVELS AFTER INTRAGASTRIC (p.o.) AND INTRAPERITONEAL (i.p.) ADMINISTRATION TO NORMOGLYCAEMIC RATS

Treatment	Route	Plasma glucose (g/L) at time (min) after treatment					
		0	20	60	120	240	360
Control	p.o.	0.99 ± 0.05	0.99 ± 0.08	0.98 ± 0.09	0.90 ± 0.16	0.95 ± 0.06	0.96 ± 0.07
(saline. 10 mL/kg)	i.p.	0.98 ± 0.04	0.96 ± 0.06	0.89 ± 0.08	0.93 ± 0.09	0.93 ± 0.08	0.94 ± 0.08
Glibenelamide	p.o.	0.96 ± 0.09	0.69 ± 0.11*	0.46 ± 0.07‡	0.57 ± 0.07†	0.73 ± 0.06	0.83 ± 0.05
(o.13 mg/kg)	i.p.	0.98 ± 0.08	0.73 ± 0.1*	0.48 ± 0.06‡	0.63 ± 0.05†	0.75 ± 0.06*	0.93 ± 0.13
Metformin	P.o.	0.99 ± 0.05	0.73 ± 0.06*	0.65 ± 0.1*	0.54 ± 0.08†	0.75 ± 0.06*	0.93 ± 0.13
(11.3 mg/kg)	i.p.	0.93 ± 0.04	0.79 ± 0.05*	0.57 ± 0.06‡	0.71 ± 0.05*	0.74 ± 0.05	0.80 ± 0.05
P.erioptera	p.o.	0.93 ± 0.05	0.59 ± 0.06‡	0.58 ± 0.14‡	0.51 ± 0.07‡	0.83 ± 0.13	1.02 ± 0.06
(0.7 g/kg)	i.p.	0.98 ± 0.07	0.68 ± 0.06‡	0.56 ± 0.22‡	0.54 ± 0.19‡	0.63 ± 0.09†	0.67 ± 0.08†

[a]Values are mean ± SEM, n = 8. *p < 0.05; †p < 0.01; ‡p < 0.001 *vs.* control; Anova and Newman – Keuls (test).

TABLE-2
PLASMA INSULIN IN NORMOGLYCAEMIC RATS AFTER INTRAGASTRIC (p.o.) AND INTRAPERITONEAL (i.p.) ADMINISTRATION OF *P. erioptera*

Treatment	Route	Insulinemia (uIU/mL) at time (min) after treatment					
		0	20	60	120	240	360
Control	P.o.	58.08 ± 4.41	68.56 ± 10.26	63.11 ± 8.42	56.64 ± 11	60.06 ± 10	73.32 ± 6.16
(saline. 10 mL/kg)	i.p.	88.88 ± 14.96	71.89 ± 8.25	60.41 ± 7.89	61.57 ± 9.15	67.27 ± 8.01	84.94 ± 7.91
P. erioptera	p.o.	82.06 ± 14.35	68.96 ± 8.52	54.14 ± 9.56	51.88 ± 3.03	63.17 ± 19.04	75.03 ± 19.42
(0.7 g/kg)	i.p.	64.22 ± 8.56	78.07 ± 12.62	90.19 ± 7.16*	73.02 ± 16.9	121.42 ± 10.01‡	113.37 ± 20.52†

[a]Values are mean ± SEM, n = 8; *p < 0.01; ‡p < 0.001 *vs.* Control; Anova and Newman – Keuls test.

TABLE-3
EFFECT OF *P. erioptera* ON PLASMA GLUCOSE LEVELS AFTER INTRAGASTRIC (p.o.) AND INTRAPERITONEAL (i.p.) ADMINISTRATION TO ALLOXAN-DIABETIC RATS[a]

Treatment	Route	Plasma glucose (g/L) at time (min) after treatment					
		0	20	60	120	240	360
Control	P.o.	2.82 ± 0.2	2.57 ± 0.14	2.14 ± 0.72	2.20 ± 0.45	2.35 ± 0.39	3.00 ± 0.48
(saline. 10mL/kg)	i.p.	2.71 ± 0.2	2.61 ± 0.18	2.59 ± 0.65	2.15 ± 0.5	2.28 ± 0.49	2.92 ± 0.51
Glibenclamide	p.o.	2.88 ± 0.2	2.15 ± 0.26	1.44 ± 039†	0.91 ± 0.08‡	1.44 ± 022‡	1.70 ± 0.34†
(0.13 mg/kg)	i.p.	3.01 ± 0.03	2.36 ± 0.35	1.21 ± 0.47*	0.88 ± 0.11*	1.44 ± 0.22*	1.70 ± 0.34
Metformin	p.o.	2.96 ± 0.1	2.66 ± 0.2	1.21 ± 0.09†	0.99 ± 0.06†	1.37 ± 0.25†	2.00 ± 0.47
(11.3 mg/kg)	i.p.	3.01 ± 0.09	1.30 ± 0.4	0.74 ± 0.41*	1.63 ± 0.25*	1.50 ± 0.35*	1.80 ± 0.30*
P.erioptera	p.o.	2.90 ± 0.08	2.02 ± 0.53*	1.05 ± 0.16‡	1.01 ± 0.07‡	1.03 ± 0.12‡	0.92 ± 0.20†^{y,x}
(0.7 g/kg)	i.p.	2.86 ± 0.3	1.74 ± 0.25†	1.60 ± 0.22†	0.79 ± 0.3‡	1.18 ± 0.21‡	1.32 ± 0.19‡^{b,x}

[a]Values are mean ± SEM, n = 8. *p < 0.05; †p < 0.01; ‡p < 0.001 *vs.* control; ^{b}p < 0.05 *vs.* glibenclamide; ^{x}p < 0.05; ^{y}p < 0.01 *vs.* metformin; Anova and Newman – Keuls test.

TABLE-4
BLOOD GLUCOSE IN GLUCOSE LOADED (0.25 g/kg) RATS BEFORE AND AFTER THE INTRAVENOUS ADMINISTRATION OF *P. erioptera*

Treatment	Blood glucose (g/L) at time (min) after load							
	0	5	10	20	30	40	50	60
Control (o.25 g/kg glucose)	0.99 ± 0.08	1.26 ± 0.08	1.47 ± 0.11	1.59 ± 0.14	1.71 ± 0.09	1.69 ± 0.11	1.46 ± 0.08	1.33 ± 0.07
P. erioptera (0.7 g/kg)	0.98 ± 0.09	1.15 ± 0.1	1.35 ± 0.06	1.48 ± 0.1	1.51 ± 0.08*	1.31 ± 0.1†	1.25 ± 0.11†	1.16 ± 0.13‡

[a]Values are mean ± SEM, n = 5. *p < 0.05; †p < 0.01; ‡p < 0.001 *vs.* control; Anova and Newman – Keuls test.

On the other hand, no variation in blood insulin level was found in normal rats orally treated with the PA extract. When compared with the control, *P. erioptera* (Table-3) significantly reduced the blood glucose levels in diabetic rats. The maximum decrease observed 2 h after the administration in plasma glucose level recorded as [1.01 g/L (- 69.96 %) and 0.79 g/L (-53.29 %), respectively after oral and i.p. treatment.

In a glucose tolerance test, intravenous treatment with *P. erioptera* significantly reduced at time intervals of 30, 40, 50 and 60 min and the increase in plasma glucose level induced by a glucose load administration (Table-4). Glycaemic values returned to basal levels more rapidly than in control group. The coefficient of glucose assimilation (KG) showed significant increase in treated rats compared to control (8.17×10^{-3} *vs.* 6.96×10^{-3}).

In conclusion, *P. erioptera* showed hypoglycemic effect in normoglycemic and hyperglycemic rats after both oral and intraperitoneal administration. The effect could be comparable to that of well known hypoglycemic compounds like metformin and glibenclamide used at 11.3 and 0.13 mg/kg, respectively. As far as the mechanism of action is concerned, in the light of the obtained results it can be speculated that *P. erioptera* activity could be due to an enhancement of peripheral metabolism of glucose. An increase of insulin release cannot be excluded. Further studies to identify the active constituents of *P. erioptera* and their mechanism of action are in progress.

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