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ORIGINAL ARTICLE

Assessment Of *Polyalthia Longifolia* Var. *Pendula* For Hypoglycemic And Antihyperglycemic Activity

Nair R, Shukla V , Chanda S

ABSTRACT

The hypoglycemic and antihyperglycemic activity of various solvent extracts of *Polyalthia longifolia* var. *pendula* leaf extracts was evaluated in alloxan induced experimental diabetes in rats. Diabetes was induced using 180 mg/kg i.p. of alloxan consecutively two times at an interval of 24 h. The test drugs were administered for 7 days. On 8th day various biochemical parameters like serum cholesterol, serum urea, serum creatinine, serum triglyceride, total serum protein, serum alkaline phosphatase, blood glucose and glycogen from liver were estimated. *Polyalthia longifolia* extracts and powder produced glucose lowering activity. However, the extracts did not modify any of the biochemical parameter significantly. Hence the extracts and crude powder are devoid of anti-diabetic properties, but has gross glucose lowering properties. The presence of anti-hyperglycemic effect against sucrose loading induced hyperglycemia is a significant finding. Now-a-days, it is considered that this effect is most important property in a drug used in diabetes treatment.

Key words: *Polyalthia longifolia*, alloxan diabetic rats, hypoglycemic activity, sucrose tolerance test, biochemical parameters

Introduction

Diabetes is defined as a state in which homeostasis of carbohydrate and lipid metabolism is improperly regulated by insulin. This results primarily in elevated fasting and post prandial blood glucose levels. If this imbalanced homeostasis does not return to normalcy and continues for a protracted period of time, it leads to hyperglycemia that in due course turns into a syndrome called diabetes mellitus (DM). DM is a group of metabolic diseases characterized by hyperglycemia, hypertriglyceridaemia, resulting from defects in insulin secretion or action or both [1]. Diabetes mellitus is a non-communicable disease, which is considered one of the five leading causes of death in the world.

Many investigations of oral anti-hyperglycemic agents of plant origin used in traditional medicine have been conducted and many of the plants show positive activity [2],[3]. Further, most of the hypoglycemic agents used in allopathic medicines are reported to have side effects in the long run [4]. Therefore, there is need to search for effective and safe drugs for diabetes.

Polyalthia is a large genus of shrubs and trees distributed in tropics and subtropics [5]. It belongs to the family Annonaceae [6], which comprises 120 genera and more than 2000 species. *Polyalthia longifolia* (Sonn.) Thw. var. *pendula* is a tall, handsome, evergreen tree with a straight trunk and horizontal branches is a native of Sri Lanka and cultivated all over Indo-Pakistan subcontinent [5]. It is locally known as Seedha Ashok. The ethnopharmacological claims for *Polyalthia longifolia* include the use of its bark as a febrifuge. It depressed the heart, lowered blood pressure and

Corresponding Author Chanda S

Phytochemical, Pharmacological and Microbiological Laboratory,
Department of Biosciences, Saurashtra University, Rajkot-360 005,
Gujarat, India
Email:sumitrachanda@yahoo.com

stimulated respiration [7]. The fungicidal effect of *P. longifolia* has also been reported by many workers [8],[9].

The present investigation was aimed in studying the hypoglycemic and anti-hyperglycemic effects of *Polyalthia longifolia* (Sonn.) Thw. var. *pendula* leaf extracts in rats.

Materials and Methods

Preparation of plant extracts

The *P. longifolia* leaves were collected from Panchayat nagar area of Rajkot, Gujarat, India and authenticated at Biosciences department of Saurashtra University, Rajkot, Gujarat (Voucher No. PSN 4). The leaves were dried, pulverized into dry powder and stored in air tight bottles. 10 g of dried leaf powder was extracted using three different solvents 1,4-dioxane, methanol and acetone. The solvent was evaporated under reduced pressure and the extracted compound was stored in air tight bottles at below 4 °C.

Animals

Wistar strain albino rats were obtained from the animal house of Sarabhai Research Centre (SRC), Baroda and in house colony was maintained at the animal house of Department of Biosciences, Saurashtra University, Rajkot. The animals were maintained on Navchakan Oil Mills, Amruth Brand rat pellet feed and tap water given ad-libitum in a normal uncontrolled condition (Exposed to natural day and night order). The rats were kept for one week for acclimatization before the experimental sessions. The studies were done after obtaining the approval of Institution ethics committee as per CPCSEA guidelines.

Hypoglycemic activity of *Polyalthia longifolia* var. *pendula*

Prior to the experimental evaluation of test drugs in diabetic rats, a study was undertaken to test its effect on fasting blood glucose level in normal rats. Animals were divided into five groups each consisting of 6 animals of either sex. One group was kept as control and the other four groups as test drug groups. Rats were fasted overnight for 15 h. Fasting blood glucose level was measured with the help of one touch glucometer. Blood was collected from the retro-orbital plexuses puncturing with the help of sterile capillaries under ether anesthesia. After collecting the fasting blood, distilled water was administered to the control group. Suspensions of *P. longifolia* leaf and its extracts were administered to the other four groups at a dose of

300mg/kg body weight orally with gastric catheter. The dose form of the powder was prepared as a suspension in distilled water. After 1 h, 2 h, 3 h and 4 h of drug/vehicle administration, the blood glucose levels were measured again with glucometer.

Effect of *P. longifolia* in Sucrose tolerance test (STT)

Modified GTT was carried out on normal rats by using sucrose. Albino rats of either sex were selected, numbered and weighed. They were divided into five groups with six animals in each group, one group serving as control and others as test drug groups. Initial blood glucose level of each rat was measured. Then the drug/vehicle was administered to the respective group. After 1 hour of drug/vehicle administration the sucrose was administered at a dose of 40 gm/kg body weight to all the five groups. The blood glucose level was estimated at intervals of 1 h, 2 h, 3 h and 4 h respectively after sucrose load. In all the animals, blood was drawn from the retro-orbital plexuses of rat by puncturing it with sterile capillaries of same bore under ether anesthesia. The glucose level was estimated by using one touch glucometer (Johnson & Johnson).

Alloxan Induced Diabetes Mellitus

Rats of either sex were taken for the study and were weighed. Their initial blood glucose level was estimated. Alloxan was administered at a dose of 180 mg/kg i.p. consecutively two times at an interval of 24 h. Forty eight hours after the 1st dose of alloxan, the glucose level was estimated. The rats with the blood glucose level ranging between 250mg/dL - 550mg/dL were selected for experimental study. After induction of diabetes, the diabetic rats were subjected to treatment on the 2nd day after induction.

The animals were grouped into 6 groups with 6 animals of either in each group. The weight of animals ranged from 200-250 g. First group of diabetic control was given distilled water. The second group was given suspension of 1, 4-dioxane extract, third group was given suspension of methanol extract, fourth group was given suspension of acetone extract, fifth group was given the dose of *P. longifolia* leaf and the sixth group was given the dose of Glipizide (0.5 mg/kg).

The diabetic rats of either sex were weighed, divided into six groups, with six animals in each group. The control group was administered distilled water as vehicle; the dioxane group (PDE) was

administered suspension of leaf extract of *P. longifolia* at a dose of 300 mg/kg body weight (p.o.) daily for a period of 7 days with the help of gastric catheter/feeding tube. In the same way, the methanol group (PME), the acetone group (PAE), the crude group (PCR) were administered suspension of leaf extract of *P. longifolia* at a dose of 300 mg/kg body weight. The standard group were administered the suspension of glipizide at a dose of 500 µg/kg body weight. On the 8th day of treatment, they were sacrificed by stunning and severing of neck blood vessels. Blood was collected during sacrifice of the animals for biochemical investigations like cholesterol [10], urea [11], creatinine [12], triglyceride [13], total protein [14], alkaline phosphatase [15] and blood glucose [10]. Samples of liver were collected and stored in fridge for estimation of glycogen [16].

Statistical Analysis

The results are expressed as Mean ± SEM. Comparison between the groups was made by students t-test and ANOVA, followed by Dunnett's t-test as per suitability P<0.05.

effect [Table/Fig 2]. The results of various biochemical parameters studied are shown in [Table/Fig 3]. The level of triglyceride was more in all the extracts as compared to the control, though the level varied, maximum being in PCR (P<0.05), which was more than the standard. The cholesterol content decreased in all the extracts as compared to the control, maximum decrease was in PAE. The glycogen content was less in control and standard while in all other groups the content showed increased levels.

The alkaline phosphatase content and creatinine content showed varied levels of either increase or decreased levels as compared to control. No consistency was observed. Protein and urea content was almost same or showed slight decreased levels as compared to control.

Alloxan, a β-cytotoxin is known to induce chemical diabetes in a wide variety of animal species damaging the insulin secreting cells [17]. Induction of diabetes by alloxan administration is indicated by rising levels of blood glucose and fall in liver

Table/Fig 1

Sr. No.	Treatment mg/kg	% Change in Glucose levels at 1 h	% Change	% Change in Glucose levels at 2 h	% Change	% Change in glucose levels at 3 h	% Change	% Change in glucose levels at 4 h	% Change
1.	Control	1.46 ± 1.12	-	15.41 ± 6.50	-	16.00 ± 5.62	-	23.17 ± 6.27	-
2.	PDE-300	0 ± 0	100	0.17 ± 0.17**@@	98.89	0 ± 0*@	100	0 ± 0**@@@	100
3.	PME-300	4.07 ± 3.45	178.76	2.29 ± 1.57@	85.13	2.85 ± 2.86@	82.18	2.85 ± 2.86*@@	87.69
4.	PAE-300	0.89 ± 0.89	39.04	0.29 ± 0.29*@@	98.11	6.13 ± 3.45	61.68	2.17 ± 2.18**@@	90.63
5.	PCR-300	8.68 ± 2.33*@	494.52	1.58 ± 0.83*@@	89.74	13.62 ± 4.98	14.87	3.83 ± 1.78*@@	83.47

Values are Mean ± SEM, n = 6 ; PDE = dioxan extract, PME methanol extract, PAE = acetone extract and PCR = crude extract P< (0.05*, 0.01**), F< (0.05[#]), ^dP<(0.05[@], 0.01^{*@}, 0.001^{**@@}) (^dP - Dunnet's t-test)

Hypoglycemic effect of *Polyalthia longifolia* leaf powder and its extracts on albino rats

Results and Discussion

The hypoglycemic effect of *P. longifolia* is shown in [Table/Fig 1]. In the control group sucrose administration induced bi-phasic hyperglycemic

glycogen [18] and as a corollary to these, significant increases in plasma cholesterol and triglycerides have been noted [19].

Table/Fig 2

Sr. No.	Treatment (mg/kg)	% Change in Glucose levels at 2 h	% Change	% Change in Glucose levels at 4 h	% Change	% Change in glucose levels at 8 h	% Change	% Change in glucose levels at 24 h	% Change
1.	Control	48.18 ± 3.11	-	28.22 ± 5.01	-	71.38 ± 11.04	-	34.24 ± 6.11	-
2.	PDE-300	46.39 ± 5.67	3.71	41.23 ± 10.42	46.10	29.46 ± 11.73* [@]	58.72	9.22 ± 4.87** [@]	73.07
3.	PME-300	8.14 ± 5.28** [@]	83.10	30.15 ± 5.96	6.83	5.13 ± 2.93*** [@]	92.81	0 ± 0*** [@]	100
4.	PAE-300	20.67 ± 9.71* [@]	57.09	43.50 ± 5.39	54.14	27.36 ± 7.19** [@]	61.66	27.01 ± 6.55	21.11
5.	PCR-300	48.71 ± 12.67	1.10	69.59 ± 15.77* [@]	146.59	28.76 ± 10.17* [@]	59.70	18.34 ± 9.33	46.43

Values are Mean ± SEM, n = 6 PDE = dioxan extract, PME methanol extract, PAE = acetone extract and PCR = crude extract

P < (0.05*, 0.01**, 0.001***), F < (0.05[#]), ^dP < (0.05[@], 0.01^{@@}, 0.001^{@@@})
(^dP – Dunnet's t-test)

Antihyperglycemic activity of *Polyalthia longifolia* leaf powder and its extracts on oral sucrose loaded albino rats

Table/Fig 3

Sr. No.	Treatment (mg/kg)	Glucose level (mg/dL)	Triglyceride Level (mg/dL)	Cholesterol Level (mg/dL)	Glycogen Level (mg/100mg wet tissue)	Alkaline Phosphatase Level (AU/dL)	Creatinine Level (mg/dL)	Urea Level (mg/dL)	Protein Level (g/dL)
1.	Control	435.55 ± 22.45	140.37 ± 5.83	82.92 ± 7.54	0.42 ± 0.11	46.70 ± 1.87	0.0074 ± 0.0005	23.88 ± 2.72	7.66 ± 0.15
2.	PDE-300	390.43 ± 78.42	150.60 ± 11.99	77.82 ± 8.11	0.75 ± 0.18	99.76 ± 37.67	0.0083 ± 0.0007	22.5 ± 3.02	7.75 ± 0.28
3.	PME-300	306.78 ± 69.53	156.83 ± 5.78	83.59 ± 2.27	0.64 ± 0.10	51.25 ± 9.64	0.0075 ± 0.0002	25.72 ± 1.43	7.37 ± 0.23
4.	PAE-300	389.98 ± 6.76	144.27 ± 10.96	68.11 ± 4.35	0.80 ± 0.14	31.26 ± 6.31*	0.0066 ± 0.0004	17.72 ± 1.48	7.33 ± 0.07
5.	PCR-300	391.71 ± 31.78	162.04 ± 6.91*	69.70 ± 2.84	0.70 ± 0.19	38.01 ± 6.23	0.0079 ± 0.0006	17.81 ± 0.87	7.32 ± 0.11
6.	Glipizid e-0.5	369.66 ± 50.01	143.53 ± 6.23	77.74 ± 8.56	1.11 ± 0.23* [@]	43.84 ± 6.92	0.0081 ± 0.0004	18.57 ± 1.76	7.44 ± 0.04

Values are Mean ± SEM, n = 6, P < (0.05*), F < (0.05[#]), ^dP < (0.05[@]), (^dP – Dunnet's t-test)

PDE = dioxan extract, PME methanol extract, PAE = acetone extract and PCR = crude extract

Antihyperglycemic activity of *Polyalthia longifolia* leaf powder and its extracts on alloxan induced hyperglycemic rats

Clinically, it has been observed that there is a presence of altered fat metabolism in type-1 and type-2 diabetes leading to an altered serum cholesterol and triglyceride levels. In various rodent models it was shown that α -glucosidase inhibitors may produce a dose dependent reduction in serum cholesterol and free fatty acids concentrations [20]. The observed activity is not significant; hence the extracts may not have significant influence on the altered lipid metabolism. The extracts were able to elevate the glycogen content which indicates that the extracts are able to induce glycogenesis in diabetic rats.

The activities of aminotransaminases in the serum are useful indicators of liver damage in the diagnosis and study of acute hepatic disease; these enzymes are located not only in the liver but also in the extra hepatic tissues [21]. The high elevation in alkaline phosphatase level in PDE may be due to degenerative condition in the liver. Damage to the structural integrity of liver is reflected by an increase in the levels of serum transaminases because these are cytoplasmic in the location and are released into circulation after cellular damage. Therefore from the results, it is reflected that PAE is able to prevent the loss of structural integrity of liver in diabetic rats. The high elevation in creatinine in PDE may be due to degenerative condition in the kidney which has lead to high rise of creatinine in serum. The high elevation in total protein in PDE may be due to degenerative condition in the muscles which has lead to rise of total protein in serum. The high elevation in urea in PME may be due to degenerative condition in the kidney which has lead to rise of urea in serum.

The extracts and crude powder of *P. longifolia* are devoid of anti-diabetic properties, but it has gross glucose lowering properties that may be established by other sets of experiments. The extracts did not modify any of the biochemical parameter significantly. The presence of anti-hyperglycemic effect against sucrose loading induced hyperglycemia is a significant finding. Now-a-days, it is considered that this effect is most important property in a drug used in diabetes treatment.

Conflict of Interest: None declared

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