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### Antihyperglycemic and hypoglycemic effect of *Portulaca quadrifida* Linn.

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#### ABSTRACT

The hypoglycemic effect of ethanolic extract of *Portulaca quadrifida* was investigated on glucose loaded and streptozotocin induced diabetic rats. The blood glucose levels were measured at 0, 1, 2 and 3 h after the treatment. The ethanolic extract of *P. quadrifida* (200 mg/kg) reduced the blood glucose of normal rat from 85.33±1.79 to 65.17±3.67 mg/dl, 3 h after oral administration of the extract (P<0.001). It also significantly lowered blood glucose level in streptozotocin induced diabetic rat from 330.67±3.27 to 132.17±4.49 mg/dl, 3 h after oral administration of the extract (P<0.001). The antihyperglycemic activity of *P. quadrifida* was compared with tolbutamide, an oral hypoglycemic agent.

**Keywords:** *Portulaca quadrifida*; Antihyperglycemic; Hypoglycemic; Streptozotocin

#### INTRODUCTION

Diabetes mellitus is a group of metabolic disorders characterized by hyperglycemia. These metabolic disorders include alteration in the carbohydrate, fat and protein metabolism associated with absolute or relative deficiencies in insulin secretions and/or insulin action. The characteristic symptoms of diabetes are polyuria, polydipsia, polyphagia, pruritis, and unexpected weight loss. Besides hyperglycemia, several other factors including dislipidemia or hyperlipidemia are involved in the development of micro and macrovascular complications of diabetes, which are

the major causes of morbidity and death [1]. There is an increasing demand by patients to use the natural products with antidiabetic activity due to side effects associated with the use of insulin and oral hypoglycemic agent such as sulfonylureas, metformin,  $\alpha$ -glucosidase inhibitors, troglitazone, etc [2-5]. The available literature shows that there are more than 400 plant species showing hypoglycemic activity [6-8] and presently several laboratories are involved in isolating new herbal hypoglycemic agents. Though some of the plants are reputed in the indigenous system of medicine for their activities, it remains to be scientifically established.

*Portulaca quadrifida* Linn. a prostrate fleshy annual or stoloniferous perennial herb with somewhat base but sometimes with simple main stems, 5-40 cm tall and generally widespread in warm countries. *Portulaca quadrifida* Linn. belongs to the family portulacaceae. It is a small diffused, succulent, annual herb found throughout the tropical parts of India. It is used as a vegetable and also used for various curative purposes. It is said to be useful in asthma, cough, urinary discharges, inflammations and ulcers. A poultice of the plant is applied in abdominal complaints, erysipelas and haemorrhoids [9]. *Portulaca quadrifida* Linn. has been reported to possess antifungal activity against *Aspergillus fumigates* and *Candida albicans* [10] and the neuropharmacological activities were reported by Syed et al [11]. The present study focused to evaluate ethanolic extracts of *P. quadrifida* in normal and streptozotocin-induced diabetic rats.

## MATERIALS AND METHODS

### Plant material

The aerial parts of the plant were collected from the foothill of Yercaud, Salem, in the month of June 2015 and cleaned to remove the debris. The collected plant was identified and authenticated by a botanist Dr. A. Marimuthu, Department of Botany, Government Arts College, Attur. A voucher specimen (PQM-1) has been kept in our museum for future reference. The plant parts were dried at room temperature for 10 d and coarsely powdered with the help of a hand-grinding mill and the powder was passed through sieve No. 60.

### Preparation of the extract

The powder of aerial parts of *P. quadrifida* was extracted separately by continuous hot extraction process using soxhlet apparatus with different solvents in increasing order of polarity from petroleum ether, chloroform, acetone, alcohol, to finally chloroform:water. After extraction, the extracts were concentrated under reduced pressure in tared vessel. The marc of crude drug powder was then once again subjected to successive extraction with other solvents and the extractive values were calculated with reference to the air-dried drug. The dry extracts were subjected to various chemical

tests to detect the presence of different phytoconstituents.

### Animals

Swiss albino mice of either sex and of approximately the same age weighing about 20-30g were used for the study. They were housed in polypropylene cages and fed with standard chow diet and water ad libitum. The animals were exposed to alternative cycle of 12 h of darkness and light each. Before each test, the animals were fasted for at least 12h. The experimental protocols were subjected to the scrutiny of the institutional animal ethics committee and were cleared by the same.

### Acute toxicity studies

The acute toxicity studies were conducted as per the guidelines of OECD (guideline 423). and were observed for mortality till 48 h and the LD<sub>50</sub> was calculated.

### Induction of diabetes

Animals were allowed to fast 24 h and were injected with freshly prepared streptozotocin solution (45 mg/kg, i.p.) as reported previously [12]. After a week, rats with marked hyperglycemia (fasting blood glucose >300 mg/dl) were employed for the study.

### Effect of *P. quadrifida* on glucose tolerance in rats

Fasted rats were divided into three groups of six each. First group served as a control and received distilled water. Group II and III received ethanolic extract of *P. quadrifida* at an oral dose of 200 mg/kg and 100 mg/kg of tolbutamide, an oral hypoglycemic agent, respectively. After 30 min of extract administration, the rats of all groups were orally treated with 2 g/kg of glucose solution [13]. Blood samples were collected from the tail vein just prior to glucose administration and at 30, 60, 90 and 120 min after glucose loading. The blood glucose level was determined by the O-toluidine method of Fings et al [14].

### Effect of *P. quadrifida* on normal and streptozotocin induced hyperglycemia in rats

Different groups of rats were used to study the effect of alcoholic extract of *P. quadrifida*. The rats were divided into five groups each consisting of 6

rats. First and second groups were served as untreated normal and untreated diabetics and fed on distilled water alone. Third and fourth groups were normal rats and diabetic rats respectively, treated with ethanolic extract (200 mg/kg) of *P. quadrifida*. Fifth group was diabetic rats treated with 100 mg/kg of tolbutamide, an oral hypoglycemic agent. After an overnight fast, the plant extract suspended in 5% gum acacia was fed by gastric gavage. Blood samples were collected for the measurement of blood glucose from the tail

vein at 0, 1, 2 and 3 h after feeding the plant extracts. The blood glucose level was determined by the O-toluidine method of Fings *et al* [14].

### Statistical analysis

All values were expressed as mean ±SEM. The data were statistically analyzed using one way ANOVA followed by Newman Keul's multiple range test and difference below P< 0.05 are considered as significant.

**Table 1: Effect of ethanolic extract of *P. quadrifida* on oral glucose tolerance in rats**

Groups	Dose (mg/kg)	Fasting blood glucose (mg/dl) after the treatment				
		0 min	30 min	60 min	90 min	120 min
Control	-	84.17±1.07	156.33±1.35	134.33±1.64	118.83±2.43	106.50±2.22
Ethanolic extract of <i>P. quadrifida</i>	200	84.17±1.19	125.33±1.26*	113.83±1.55*	99.50±2.26*	84.50±1.81*
Tolbutamide	100	86.17±1.32	113.33±2.19*	91.33±2.05*	81.17±1.83*	78.33±2.04*

Values are expressed as mean ± SEM, n=6, \* P<0.001 when compared with control.

**Table 2: Effect of ethanolic extract of *P. quadrifida* on fasting blood glucose levels (mg/dl) in normal and diabetic rats**

Groups	Dose (mg/kg)	Fasting blood glucose at different hours after the treatment			
		0 h	1 h	2 h	3 h
Untreated normal	-	84.17±1.19	85.33±1.31	85.17±1.55	86.17±1.88
Treated normal	200	85.33±1.79	74.33±2.04	71.83±2.20*	65.17±3.67*
Untreated diabetics	-	332.50±7.11	334.33±6.53	338.67±5.22	340.50±3.51
Treated diabetics	200	330.67±3.27	224.33±5.23	196.83±8.49*	132.17±4.49*
Tolbutamide	100	328.67±5.22	185.50±4.98	130.33±5.72*	112.67±4.41*

Values are expressed as mean ± SEM, n=6, \* P<0.001 when compared with control.

## RESULTS

The plant *P. quadrifida* was collected from the foothill of Yercaud, Salem, air-dried and extracted by continuous hot extraction process using soxhlet apparatus. The average percentage yield of ethanolic extract of *P. quadrifida* was found to be 3.8 % w/w. The LD<sub>50</sub> was found to be 2000 mg/kg for ethanolic extract of *P. quadrifida*. The ethanolic extract did not exhibit and toxic effects up to 1000 mg/kg when administered to mice as a single i.p. dose.

The effect of *P. quadrifida* on glucose tolerance is reported in Table 1. The ethanolic extract of *P. quadrifida* has prevented the increase in blood glucose levels significantly (P<0.001) after glucose administration and the maximum glucose tolerance was observed at 120 min.

The effect of ethanolic extract of *P. quadrifida* on fasting blood glucose level was assessed in normal and diabetic rats at various time intervals are shown in Table 2. The mean blood glucose level decreased from 85.33±1.79 to 65.17±3.67 mg/dl in rats treated with ethanolic extract of *P. quadrifida* (P<0.001). A significant decrease in blood glucose level was observed in the diabetic group treated with *P. quadrifida* from an initial level of 330.67±3.27 to 132.17±4.49 mg/dl, 3 h after administration, which is comparable to that of effect of 100 mg/kg of tolbutamide.

## DISCUSSION

In this study the **ethanolic** extract of *P. quadrifida* at the dose of 100 mg/kg produced a significant fall in the blood glucose level in both

normal and diabetic rats and this was evident 1 h after the administration of the extracts. On the other hand, tolbutamide caused significantly more hypoglycemia in comparison with the plant extract. An emphasis is laid on glucose homeostasis as a severe hypoglycemia can result in life threatening situation. Therefore, lesser hypoglycemia with plant extract in comparison with tolbutamide is a desirable feature. The mechanism of this hypoglycemic effect of the extracts is not elucidated in this study. Some medicinal plants with hypoglycemic properties are known to increase circulating insulin level in normoglycemic

rats [15]. A possible mechanism of action is that the extract might have stimulated residual pancreatic mechanism, probably increasing peripheral utilization of glucose as postulated by Erah et al[16] to explain hypoglycemic effect of the extracts of *P. quadrifida*. Further investigation is expected to characterize the active hypoglycemic principle and to elucidate the mechanism of action. In our studies the alcoholic extract of *P. quadrifida* produced the maximum glucose lowering activity in diabetic rats after 3 h and both extracts produced significant hypoglycemic activity in normal rats.

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