

Short Communication

Antihyperglycemic effect and phytochemical screening of aqueous extract of *Passiflora foetida* (Linn.) on normal Wistar rat model

M. A. Siriwardhene¹, A. M. Abeysekera³, U. G. Chandrika^{2*} and A. K. E. Goonetilleke¹

¹Department of Pharmacology, University of Sri Jayewardenepura, Gangodawila, Nugegoda, Sri Lanka.

²Department of Biochemistry, University of Sri Jayewardenepura, Gangodawila, Nugegoda, Sri Lanka.

³Department of Chemistry, University of Sri Jayewardenepura, Gangodawila, Nugegoda, Sri Lanka.

Accepted 4 November, 2013

***Passiflora foetida* L. belonging to family Passifloraceae is used in Sri Lanka as a traditional medicine in the treatment of diabetes mellitus. This study was designed to examine the antihyperglycemic activity of the aqueous leaf extract of *P. foetida* in normoglycemic Wistar rats. The extract at a dose of 433 mg/kg (calculated on the basis of the traditional raw salad intake per meal) had a effect not significantly different ($p < 0.05$) for glipizide at a dose of 10 mg/kg, 90 min after the glucose load. Preliminary phytochemical screening indicated the presence of flavonoids, steroids and saponins as major constituents.**

Key words: *Passiflora foetida*, anti-hyperglycaemic effect, glipizide.

INTRODUCTION

Diabetes mellitus (DM) is a metabolic disease associated with elevated blood glucose levels. The disease is characterized by either a defect and/or a deficiency of insulin in the body (type II and I, respectively). Many regions of Asia and Africa show a high prevalence of the disease, while the incidence is increasing. According to a report by the International Diabetic Federation, East and North Africa have six of the ten countries with the highest prevalence of diabetes in the world. (IDF Diabetes Atlas, 2011). Recent estimates indicated that 171 million people in the world were suffering from diabetes in the year 2000 and this is projected to be 366 million by the year 2030 (Report of a WHO/IDF Consultation, 2008). When the prevalence of diabetes in Sri Lanka is considered, one-quarter of the affected population live in the urban areas (Wild et al., 2004).

Type II DM is currently managed by oral antihyperglycemic agents. However, gastrointestinal disturbances, hypoglycemia and disturbances with liver functions are the

common side effects with classical oral antihyperglycemic agents. During the last two decades, traditional systems of medicine and research on medicinal plants have become a topic of global interest and importance (Bailey and day, 1989; Bailey, 2002). Because of their effectiveness and minimal side effects, medicinal plants are prescribed even if their active compounds are unknown (Ivorra et al., 1989).

The leaves of *Passiflora foetida*, family Passifloraceae, is commonly used in Sri Lanka by those having type II diabetes. It is commonly known as bush passion fruit or wild passion fruit, or love-in-a-mist or passion flower or stinking passion flower (English); wal wel dodam or padawal (Sinhala), siruppunaikkali (Tamil), loliloli ni kalavo (Fijian), passiflore or passiflore fétide (French), vaine 'ae kuma and vaine 'initia (Tongan). The plant is widely distributed in all provinces in Sri Lanka.

Though the plant has drawn the attention among the traditional population as a remedy for DM in Sri Lanka,

*Corresponding author. E-mail: udumalagala2002@yahoo.com. Tel: 0094-011-2803578.

only a few reports on its pharmacological activity have been reported. The methanolic extract of *P. foetida* root has been reported to have anticancer activity in a conventional animal model of liver cancer (Balasubramaniam et al., 2010). The hepatoprotective activity of *P. foetida* fruits on CCl₄ induced swiss albino mice was also reported by Ramasamy et al. (2009). However, there is little or no scientific evidence of the antihyperglycemic activity of *P. foetida*.

Therefore, the current study was carried out to assess the antihyperglycemic effect of *P. foetida* in normoglycemic rat models and to identify the classes of major phytochemical constituents in the plant.

MATERIALS AND METHODS

Plant and extraction

Fresh leaves of the plant *P. foetida* was collected from Piliyandala, Colombo district, western province of Sri Lanka. This plant was taxonomically compared with authentic specimen at the National Botanical Gardens, Peradeniya, Sri Lanka. The herbarium sample of the plant is deposited in the Department of Pharmacology, Faculty of Medical Sciences of the University of Sri Jayewardenepura (17PH001).

The fresh leaves of *P. foetida* (100 g) were dried to a constant weight at 40°C and ground with ice using a mechanical grinder. It was then mixed with water to obtain a final volume of 1000 ml. The extraction was filtered through a gauze filter to obtain a cloudy pale yellowish filtrate.

Chemicals

Glucose was obtained from Glaxo Smithkline Beecham Ceylon Ltd, Colombo-01, Sri Lanka. Metformin hydrochloride EP (Code no. 41102, Purity 99.8%) and Glipizide USP (Code no. 41017, purity 100.8%) reference standards were obtained from Astron Pharmaceuticals Ltd, Ratmalana, Sri Lanka.

Animals

The male Wistar albino rats weighing about 250 to 300 g bred in the animal house of Medical Research Institute, Ministry of Health, Colombo 07, Sri Lanka, were used in the study. The animals were fed on a standard diet specified by WHO and water *ad libitum*. The experimental protocol was approved by the ethical committee of the Faculty of Medical Sciences, University of Sri Jayewardenepura (Approval no. 464/09). All the animals were kept and maintained under laboratory conditions of ambient temperature (25°C) maintaining 12 h (0600 to 1800 h) day and night cycle.

Experimental design for the oral glucose tolerance test (OGTT)

In the experiment, a total of 24 rats were used. The rats were divided into four groups comprising six animals in each group as follows: Group I, control (treated with 1 ml of distilled water orally); Group II, treated with metformin (as hydrochloride) at a dose of 100 mg/kg, dissolved in 1 ml of distilled water; Group III, treated with glipizide at a dose of 10 mg/kg, dissolved in 1 ml of distilled water; Group IV, treated with plant extract at a dose of 433 mg/kg, dissolved in 1 ml of distilled water.

Animals were deprived of food for 16 h before administration of the extract but allowed water *ad libitum*. A glucose solution (1.0 ml) at a dose of 2.5 g/kg (Srinivasan et al., 2005) was administered orally 30 min after each treatment.

Measurement of blood glucose

Blood glucose levels were determined before the administration of each treatment. The subsequent blood glucose levels were determined at 30, 90, 150 and 180 min after the glucose load. The blood glucose level was determined using a Bionime Glucometer (GM300, Bionime Corporation, Bionime GmbH, Switzerland).

Preliminary phytochemical screening

Dried and powdered plant materials (10 g) were extracted with 80% ethanol (50 ml) reflux for 2 h. The solvent was removed in vacuum to give the concentrated extract, which was tested for the presence of different classes of phytochemicals according to Farnsworth (1966).

Statistical analysis

All data were expressed as mean $\pm$ standard error of mean (SEM). One way analysis of variance (ANOVA) with post hoc Dunnett's multiple comparison tests were performed using GraphPad Prism version 5.00 for Windows, GraphPad Software, San Diego California USA and SPSS version 16 (SPSS, Cary, NC, Chicago). The p values of 0.05 and less were taken to imply statistical significance between the means.

RESULTS AND DISCUSSION

The oral administration of the aqueous extract of *P. foetida* leaves was used to evaluate the antihyperglycemic activity in rats, using OGTT. The plant produced antihyperglycaemic activity in rats at a dose of 433 mg/kg. The highest activity was observed at 90 min. It reduced the blood glucose level to a mean value of 96.3 ± 2.6 at 90 min (34.5% lowering of blood glucose) when compared with the mean value of 149.3 ± 3.4 obtained in the control group (Table 1).

The results of the phytochemical screening are shown in Table 2. *P. foetida* aqueous extract at a dose of 433 mg/kg body weight used in this study was based on the traditional weight average of the raw salad intake per person with a routine meal in Sri Lanka (Ethnopharmacological Survey, 2008, 2009 un-published data).

In our study, the effect of *P. foetida* leaf extract was compared with that of metformin and glipizide, two of the common oral hypoglycemic agents in use today. As metformin does not lower blood glucose levels in normoglycemic subjects (Penicaud et al., 1989), it did not have a significant antihyperglycemic effect as expected, confirming the validity of the model. Whereas glipizide at 10 mg/kg brought about a significant ($p < 0.05$) lowering of blood glucose. At the time of the highest activity (90 min), there was no significant ($p < 0.05$) difference between the activities of glipizide at 10 mg/kg and *P. foetida* leaf

Table 1. Effect of the aqueous extract of *P. foetida* on fasting blood glucose levels (mg/dl) of normoglycaemic rats (mean $\pm$ SEM).

Treatment group	Blood glucose levels (mg/dl)				
	Initial	30 min	90 min	150 min	180 min
Group I: Control (distilled water)	90.7 $\pm$ 3.0	120.2 $\pm$ 3.3	149.3 $\pm$ 3.4	118.7 $\pm$ 1.8	98.3 $\pm$ 2.2
Group II: Metformin (100 mg/kg)	84.3 $\pm$ 2.8	117.5 $\pm$ 2.3	128.7 $\pm$ 3.3 (6.7%)	108.3 $\pm$ 5.0	94.0 $\pm$ 2.5
Group III: Glipizide (10 mg/kg)	99.2 $\pm$ 6.2	101.3 $\pm$ 5.8	95.3 $\pm$ 7.6 ^a (32.6%)	85.3 $\pm$ 5.1 ^a	99.7 $\pm$ 3.8
Group IV: <i>P. foetida</i> (433 mg/kg)	99.2 $\pm$ 1.6	112.8 $\pm$ 2.2	96.3 $\pm$ 2.6 ^a (34.5%)	98.5 $\pm$ 2.7 ^a	99.6 $\pm$ 4.0

Number of rats per group = 6. The values given in parentheses represent the percentage reduction in blood glucose when compared to distilled water. ^aP<0.05 when compared to control (distilled water).

Table 2. Classes of phytochemicals detected in the leaves of *P. Foetida*.

Phytochemical	Aqueous extract
Alkaloids	-
Saponins	++
Tannins	+
Phlobatannins	+
Steroids	++
Terpenoids	+
Flavonoids	+++
Glycosides With steroidal ring	-
Glycosides With deoxy-sugar	-
Anthraquinones	-

-, Not detected; +, present in low concentration; ++, present in moderate concentration; +++, present in high concentration.

extract at 433 mg/kg.

Several other plants used in Sri Lanka for diabetes including *Aegle marmelos* (Sharmila et al., 2004), *Cassia auriculata* (Uma et al., 2006), *Scoparia dulcis* (Latha and Peri, 2004) and *Momordica charantia* (Reyes et al., 2006) have been shown to have antihyperglycemic activities. This is the first time the antihyperglycemic effect of *P. foetida* is being reported.

The phytochemical screening indicated the presence of flavonoids, steroids and saponins. The presence of several flavonoids in *P. foetida* have been reported previously (Hara et al., 1990; Matsumoto et al., 1993; Valsa et al., 1997; Kobayashi et al., 2000).

Conclusion

The leaves of *P. foetida* possess anti hyperglycemic activity, thus supporting the ethnomedical usage of the plant. Its mode of action may be similar to that of glipizide, further work with diabetic models and mechanistic studies are under way.

ACKNOWLEDGEMENT

The authors wish to thank the University of Sri Jayewardenepura

(Research Grant No. ASP/06/PR/2008/05) and the University Grant Commission of Sri Lanka (Research Grant No. UGC/ICD/CRF 2009/1/5).

REFERENCES

- Bailey CJ (2002). Potential new treatments for type-2 diabetes. *Trends Pharmacol. Sci.* 21:259–265.
- Bailey CJ, Day C (1989). Traditional plants medicines as treatment for diabetes. *Diabetes Care* 12:553–564.
- Balasubramaniam A, Manivannan R, Emin B (2010). Anticarcinogenic effect of *Passiflora foetida* Linn root on the development of liver cancer induced by DEN in rats. *Int. J. Drug Formul. Res.* 1(2):144–151.
- Echeverri F, Arango V, Quinones W, Torres F, Escobar G, Rosero Y, Archbold R (2001). Passifloricins, polyketides alpha-pyrone from *Passiflora foetida* resin. *Phytochemistry* 56:881–888.
- Farnsworth NR (1966). Biology and Phytochemical screening of plants. *Pharm. Sci.* 55:225–276.
- Ivorra MD, Paya M, Villar A (1989). A review of natural products and plants as potential antidiabetic drugs. *J. Ethnopharmacol.* 27:243–275.
- Latha M, Peri L (2004). Effect of an aqueous extract of *Scoparia dulcis* on blood glucose, plasma insulin and some polyol pathway enzymes in experimental rat diabetes. *Braz. J. Med. Biol. Res.* 37:577–586.
- Penicaud L, Hitier Y, Ferre P (1989). Hypoglycaemic effect of metformin in genetically obese (fa/fa) rats results from an increased utilization of blood glucose by intestine. *Biochem. J.* 262:881–885.
- Ramasamy A, Balasundaram J, Sundararaman J, Rajappan M, Raju SK (2009). Effect of ethanol extract of fruits of *Passiflora foetida* Linn. on CCl₄ induced hepatic injury in rats. *J. Pharm. Res.* 2(3):413–415.
- Report of a WHO/ IDF consultation. (2008). Definition and Diagnosis of Diabetes Mellitus and Intermediate Hypoglycemia. Geneva: WHO.
- Reyes BAS, Bautista ND, Tanquilut NC, Anunciado RV, Leung AB, Sanchez GC, Magtoto RL, Castronuevo P, Tsukamura H, Maedaf K I (2006). Anti-diabetic potentials of *Momordica charantia* and *Andrographis paniculata* and their effects on estrous cyclicity of alloxan-induced diabetic. *J. Ethnopharmacol.* 105:196–200.
- Sharmila U, Shama KS, Suneetha G, Balachandra NM, Subramanya U (2004). A study of hypoglycemic and antioxidant activity of *Aegle marmelos* in alloxan induced diabetic rats. *Indian J. Physiol. Pharmacol.* 48(4):476–480.
- Srinivasan K, Viswanad B, Lydia A, Kaul CL, Ramarao P (2005). Combination of high-fat diet-fed and low-dose streptozotocin-treated rat: A model for type 2 diabetes and pharmacological screening. *Pharmacol. Res.* 52:313–320.
- Uma PD, Selvi S, Suja, Selvam K, chinnaaswamy P (2006). Antidiabetic and hypolipidemic effect of *Cassia auriculata* in alloxan induced diabetic rats. *Int. J. Pharmacol.* 6:601–607.
- Wild SG, Roglic A, Green R, King H (2004). Global prevalence of diabetes. Estimated for the year 2000 and projection for 2030. *Diabetes Care* 27:1047–1054.