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Research Article

ALPHA-AMYLASE INHIBITORY AND HYPOGLYCEMIC ACTIVITY OF *CLERODENDRONE MULTIFLORUM* LINN. STEMS

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ABSTRACT

In the present investigation, methanolic and ethyl acetate extracts of *Clerodendrum multiflorum* stems is investigated for alpha amylase in-vitro inhibitory activity and hypoglycemic effect by oral administration at different doses in rats. *Clerodendrum multiflorum* methanolic and ethyl acetate extract showed good in-vitro alpha amylase inhibitory activity as compare to standard acarbose with IC_{50} value of 25.33 and 36.86. Also the oral administration of methanolic and ethyl acetate extract at dose of 200mg/kg body weight exhibited a significant (*P< 0.01, **P< 0.05) hypoglycaemic activity in normal rats and antihyperglycemic activity in alloxan induced diabetic rats (*P< 0.01, **P< 0.05). Besides total phenolic and total flavonoids contents was also investigated for methanolic and ethyl acetate extracts. Phytochemical results revealed the presence of steroids, saponins, flavonoids, alkaloids, tannin, glycosides and reducing sugars in the extract.

Keywords: alpha-amylase inhibitory, hypoglycaemic activity, *Clerodendrum multiflorum.*

INTRODUCTION

Diabetes is a most common endocrine disorder and serious illness with multiple complications and premature mortality, accounting for at least 10% of total health care expenditure in many countries [1]. Diabetes mellitus is a metabolic disorder of multiple etiologies characterized by chronic hyperglycemia with disturbance of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action or both [2]. It affected about 171 million people worldwide in 2000 and the number is projected to increase to at least 366 million by 2030 [3]. One therapeutic approach for treating diabetes is to decrease the post-prandial hyperglycaemia. This is done by retarding the absorption of glucose through the inhibition of the carbohydrate hydrolyzing enzymes, alpha-amylase and alpha-glucosidase in the digestive tract. Inhibitors of these enzymes delay carbohydrate digestion and prolong overall carbohydrate digestion time, causing a reduction in the rate of glucose absorption and consequently blunting the post-prandial plasma glucose rise [4]. Examples of such inhibitors which are in clinical use are acarbose, miglitol and voglibose [5].

Plants continue to play an important role in the treatment of diabetes, particularly in developing countries where most people have limited resources and do not have an access to modern treatment. The increase in demand in industrially-developed countries to use alternative approaches to treat diabetes, such as plant-based medicines, is also due to the side effects associated with the use of insulin and oral hypoglycaemic agents [6]. So investigation of different plants or plant based drugs for hypoglycemia is important. And the present study was under taken to evaluate the in-vitro alpha amylase and hypoglycemic activities in normal and diabetic rats.

Clerodendrum multiflorum Linn is a large bush or small tree belonging to the family verbenaceae. It is widely distributed throughout India in the drier parts, Baluchistan and Ceylon[7] and plant is already investigated for anti-diabetic activity (leaves) [8], immunomodulatory activity [9], antiamnesic activity (bark) [10] and antiarthritic activity [11]., hepatoprotective activity [12], anti-Fungal activity [13], psychopharmacological activity [14], anti-diarrhoeal activity [15]. Dried roots and flowers of *Clerodendrum multiflorum* yielded rhamnopyrosyl(1-2)-2-D-glucopyranosyl-7-O-naringin-4-O-α and D-glucopyranoside-5-methyl ether 2,4-trihydroxy,6-methoxy chalcone-4, 4-α-D diglucoside, pectolinarigenin, hispidulin, apigenin [16]. From leaves steroid (24 s) ethylcholesta – 5, 22, 35- trine- 3 β – ol and flavonoids as scutellarein and pectolinarigenin (4', 6-dimethyl scutellarein) were isolated. Ceryl alcohol, clerodendrin, clerosterol and clerodendrin were isolated from roots. [17, 18, 19]

MATERIAL AND METHOD

Plant material

Stems of *Clerodendrum multiflorum* were collected in June 2009 from Ahmednagar district, Maharashtra (India). The plant specimen was was authenticated from Botanical Survey of India, Pune (Voucher specimen no. CKS1). Plant materials were dried under shade and coarsely powdered for extraction. The coarsely powdered stems (500g) of *Clerodendrum multiflorum* were separately subjected to extraction using ethyl acetate and methanol by maceration for 10 days. The methanolic and ethyl acetate extracts were concentrated by rotary vacuum evaporator under reduced pressure and then dried in open air.

In-vitro Alpha- amylase inhibitory activity[20]

The assay was carried out following the standard protocol with slight modifications. [21] Starch azure (2 mg) was suspended in a tube containing 0.2ml of 0.5 M Tris-Hcl buffer (pH 6.9) containing 0.01 M calcium chloride (substrate). The tube was boiled for 5 min and then pre incubated at 37°C for 5 min. 1ml of 0.1% of dimethyl sulfoxide was used to dissolve 1 mg of dried plant extract in order to obtain concentrations of 9.37, 18.75, 37.5 µg/ml. Then 0.2 ml of plant extract of a particular concentration was put in the tube containing the substrate solution. 0.1 ml of porcine pancreatic amylase in Tris-Hcl buffer (2 units/ml) was added to the tube containing the plant extract and substrate solution.

The process was carried out at 37°C for 10 min. The reaction was stopped by adding 0.5 ml of 50% acetic acid in each tube. The reaction mixture was then centrifuged at 3000 rpm for 5 min at 4°C. The absorbance of resulting supernatant was measured at 595 nm using UV spectrophotometer. Same procedure was followed for both the plant extracts (methanol and ethyl acetate) to test the alpha amylase inhibitory effects. The experiments were repeated thrice using the same protocol.

Animals

Healthy Albino male rats weighing 160-180 g were used. They were housed under standard environmental conditions of temperature, humidity and light, and provided with standard rodent food and water ad libitum. All the animals were carefully monitored and maintained in accordance with CPCSEA guidelines on control and supervision of experimental animals. The ethical clearance was obtained from the Institutional Animal Ethics Committee before the experiment.

Evaluation of extract on normal healthy rats [22]

The animals were randomly divided into seven groups of six animals each. Group I served as control and received distilled water. Groups II, III, IV, V, VI and VII received methanolic and ethyl acetate extracts orally at the dose of 100 mg/kg, 200 mg/kg, and 400 mg/kg respectively. At the end of the fasting period taken as zero time (0 h), blood was withdrawn from the tail vein under mild ether anesthesia. Serum was separated by centrifugation and glucose was estimated. Blood glucose levels were determined 30, 60, 120, 150 and 180 minutes following treatment.

Evaluation of extract in Alloxan induced diabetes

Induction of diabetes

Diabetes was induced in male albino rats, aged 4 months (body weight 160-180 g) by intraperitoneal administration of ice-cold aqueous alloxan monohydrate (150 mg/kg body weight) by the method described earlier [23]. After a fortnight, rats with marked hyperglycemia (fasting blood glucose >250 mg/dl) were selected and used for the study. All the animals were allowed free access to tap water and pellet diet and maintained at room temperature in plastic cages.

Experimental design

The rats were divided into nine groups and each group consisted of six rats.

Group I normal untreated rats

Group II diabetic untreated rats

Group III diabetic rats treated with standard Glibenclamide 0.25 mg/kg b.w.

Group IV diabetic rats treated with 100mg/kg b.w. methanolic extract.

Group V diabetic rats treated with 200mg/kg b.w. methanolic extract

Group VI diabetic rats treated with 400mg/kg b.w. methanolic extract

Group VII diabetic rats treated with 100mg/kg b.w. ethyl acetate extract

Group VIII diabetic rats treated with 200mg/kg b.w. ethyl acetate extract

Group IX diabetic rats treated with 400mg/kg b.w. ethyl acetate extract

After an overnight fast Group I and Group II rats were fed distilled water alone and for other groups the plant extract suspended in distilled water were fed to the experimental rats by gastric intubations, using a force feeding needle. Blood samples were collected for the measurement of blood glucose from the tail vein at 0, 7th, 15th and on 21st day after feeding of the plant extract once daily. Blood glucose was measured and the results were compared with those of 1st and 2nd group of rats which were treated with distilled water.

Estimation of total phenolics and total flavonoids

Total phenolic content of methanolic and ethyl acetate extracts of *Clerodendrum multiflorum* was determined by using Folin-Ciocalteu reagent [24]. The blue color formed due to the polyphenol content in the extract was measured at 760 nm using a Shimadzu UV-1601 spectrophotometer and the results were expressed as µg/mg of gallic acid equivalent. Total flavonoids of methanolic and ethyl acetate extracts of two samples were determined using the method of Liu et al. [25] with some modifications. In brief, the extract was diluted with 80% aqueous ethanol (0.9 ml).

Aliquots of 0.5 ml of extract were added to test tube containing 0.1 ml of 10% aluminum nitrate, 0.1 ml 1M aqueous potassium acetate and 4.3 ml of 80% ethanol. The reaction tubes were set aside for 40 min at room temperature. At the end of this time, optical density of each sample was determined at 415 nm using a UV spectrophotometer. Total flavonoids content was calculated by interpolation on a standard curve established with a reference standard, quercetin. Quercetin and Folin-Ciocalteu reagent were obtained from Sigma-Aldrich, Germany

Statistical analysis

All the values of body weight and fasting blood sugar were expressed as mean ± standard error of mean (S.E.M.) and analyzed for ANOVA and post hoc Dunnet's *t*-test. Differences between groups were considered significant at $p<0.05$, $p<0.01$ levels.

RESULTS AND DISCUSSION

Diabetes mellitus is one of the most serious, chronic diseases that is developing along with an increase in both obesity and ageing in the general population. One of the therapeutic approaches for decreasing post-prandial hyperglycemia is to retard absorption of glucose by the inhibition of carbohydrate hydrolyzing enzymes, for example alpha-amylase and alpha-glucosidase, in the digestive organs. We therefore investigated the inhibitory effects of a methanol and ethyl acetate extract from *Clerodendrum multiflorum* on alpha-amylase (Table 1).

The crude methanolic and ethyl acetate extract of *Clerodendrum multiflorum* showed good inhibitory activity for alpha-amylase with the IC_{50} value of 25.22 and 36.86 as compared to standard acarbose having IC_{50} value 9.22.

In the present study methanolic extract and ethyl acetate extract at 200 mg/kg significantly reduced the normal blood glucose level as compare to 100 mg/kg and 400 mg/kg dose. The results of acute hypoglycaemic activity showed significant ($p < 0.01$, $p<0.05$) increase in plasma glucose level as compare to normal control rats over the 3-h period (Table 2). The methanolic and ethyl acetate extracts of stems of *Clerodendrum multiflorum* also have shown significant ($p<0.01$, $p<0.05$) antihyperglycemic activity (Table 3). But methanolic extract showed good antihyperglycemic activity as compare to ethyl acetate extract.

Hence the methanolic extracts may be considered to have good antihyperglycemic active principles. The phytochemical screening of *Clerodendrum multiflorum* stems revealed the presence of flavonoids, phenolic compounds, sterols/triterpenoids, alkaloids, tannins. Flavonoids, sterols/triterpenoids, alkaloids and phenolics are known to be bioactive antidiabetic principles [26, 27, 28, 29]. Flavonoids are known to regenerate the damaged beta cells in the alloxan diabetic rats [30].

Phenolics are found to be effective antihyperglycemic agents [31]. In the present study, 7.11 µg/mg of flavonoids and 75.28 µg/mg phenolic compounds were found to be present in the methanolic extract of *Clerodendrum multiflorum* stems (Table 4) so it may be one of the reason that methanolic extract shows good hypoglycemic and antihyperglycemic activity.

Changes in initial and final body weight in control and experimental groups are shown in Table 5. Significant weight loss was observed in diabetic rats compared to control non-diabetic rats. Treatment with *Clerodendrum multiflorum* stems extract or glibenclamide improved the body weight as compared to normal control rats.

The antidiabetic effect of methanolic extract of *Clerodendrum multiflorum* may be due to the presence of more than one antihyperglycemic principle and their synergistic properties. In this study, the antihyperglycemic activity caused by glibenclamide in alloxan-induced diabetic rats is an indication of the presence of some beta cells, as glibenclamide is known to stimulate insulin secretion from beta cells.

The methanolic extract of *Clerodendrum multiflorum* stems may have stimulating effect on the remnant beta cells. However further studies will be focused on determination of the mechanism(s) of action, as well as on the isolation of bioactive principles. However, further experiments are required to elucidate the exact mechanism of action.

Table 1: Alpha-amylase inhibition activity of *Clerodendrum multiflorum* extracts

Sr. no.	Test extract	Dose (µg/ml)	Percent inhibition	IC_{50} (µg/ml)
1	MEC	9.37	18.90 ±0.0776	25.22
		18.75	45.04 ±0.0852	
		37.5	68.68 ±0.2967	
2	EAC	9.37	5.62 ±0.3180	36.86
		18.75	24.49 ±0.2743	
		37.5	49.71 ±0.3533	
3	Acarbose	2.5	4.99 ± 0.05292	9.22
		5	28.11 ± 0.0688	
		10	53.13 ±0.1386	

Results are expressed as ± SEM (n=3). MEC and EAC represent methanolic and ethyl acetate extracts of *Clerodendrum multiflorum.*

Table 2: Effect of methanolic and ethyl acetate extracts of *Clerodendrum multiflorum* on normal animals

Groups	Treatment (dose mg/kg)	Fasting	30 min	60 min	120 min	150min	180 min
Control group	-	80.4 ± 2.337	79.6 ± 2.379	78.8 ± 2.267	78.4 ± 2.227	77.8 ± 2.131	77.8 ± 1.908
Group IA	ME-100 mg/kg	79.0 ± 2.121	77.0 ± 1.87*1	74.6 ± 1.631*	68.2 ± 1.655*	70.6 ± 1.600*	73.8 ± 1.497*
Group IIA	ME-200 mg/kg	78.8 ± 3.513	76.8 ± 3.153*	68.6 ± 3.855*	62.4 ± 3.855*	71.2 ± 3.734*	74.8 ± 3.499*
Group IIIA	ME-400 mg/kg	75.8 ± 2.922	73.2 ± 3.216**	65.0 ± 3.347**	66.8 ± 3.121**	68.8 ± 3.121**	71.0 ± 2.775**
Group IB	EA-100 mg/kg	78.6 ± 2.874	75.6 ± 2.874*	72.0 ± 2.881*	71.0 ± 3.146*	72.8 ± 3.023*	74.6± 3.124*
Group IIB	EA-200 mg/kg	77.8 ± 2.746	76.8 ± 2.596*	67.6 ± 2.581*	64.8 ± 2.154*	73.6 ± 2.518*	74.6 ± 2.786*
Group-IIIB	EA-400 mg/kg	79.4 ± 3.326	77.6 ± 3.669**	70.0 ± 3.317**	67.0 ± 3.146**	73.8 ± 3.262**	75.6 ± 3.076*

Results are expressed as ± SEM (n=6), Data processed by one way ANOVA followed by Dunnett's test, *P< 0.01, **P< 0.05 significant when compared to control group.

Table 3: Effect of methanolic and ethyl acetate extracts of *Clerodendrum multiflorum* on diabetic animals

Group	Treatment	Blood glucose concentration in mg/dl			
		0 day	7 day	15 day	21 day
I	Control (Normal saline)	78.75 ± 2.594	78.0 ± 2.671	77.83 ± 2.845	78.91 ± 2.451
II	Diabetic control	301.83 ± 12.49	302.33 ± 12.556**	302.66 ± 12.582*	302.78 ± 11.281*
III	Glibenclamide (0.25mg/kg)	306.83 ± 9.867	241.33 ± 9.969**[a]	199.16 ± 10.394*[a]	152.21± 10.013*[a]
IV	MeOH-100mg/kg	309.33 ± 9.16	285.5 ± 9.069**	269.33 ± 9.687*	248.45 ± 9.617*
V	MeOH-200mg/kg	307.83 ± 6.28	267.83 ± 9.112**[a]	232.33 ± 6.494*[a]	201.79 ± 5.674*[a]
VI	MeOH-400mg/kg	306.0 ± 9.78	265.16 ± 6.585**[a]	240.33 ± 6.157*[a]	212.37 ±5.978*[a]
VII	EA-100mg/kg	305.5 ± 8.65	271.16 ± 9.119 **	268.0 ± 8.881*	254.10 ± 9.019*
VIII	EA-200mg/kg	304.16 ± 12.45	263.0 ± 10.066**[a]	240.83 ± 11.016*[a]	219.56 ± 10.078*[a]
IX	EA-400mg/kg	306.5 ± 8.99	268.166±12.499**[a]	243.16 ± 11.965*a	219.02 ± 11.897*[a]

Results are expressed as ± SEM (n=6), *P< 0.01, **P< 0.05 significant when compared to control group. [a]P<0.05 significant when compared to diabetic control.

Table 4 Total phenolic and flavonoids content of methanolic and ethyl acetate extract of *Clerodendrum multiflorum*

Sr. no.	Crude drug samples	Total phenolic content (µg/mg)	Total flavonoids content (µg/mg)
1	MEC	75.28 ±0.4204	7.11 ±0.2564
2	EAC	44.9 ± 0.0635	8.56 ± 0.3535

Results are expressed as ± SEM (n=3) and compared with standard as gallic acid for Total phenolic content and Quercetin for total flavonoids content.

Table 5: Changes in body weight of animals during the activity

Days	Normal group	Diabetic control	Test group-IA	Test group-IIA	Test group-IIIA	Test group-IB	Test group-IIB	Test group-IIIB
0	170.2±3.813*	170.6±3.043*	172.8 ± 2.17*	171.2± 3.40*	170.4 ± 3.61*	173 ± 2.97*	172.8 ± 2.96*	169.2 ± 3.28*
21	172.33±1.372	146.6±2.201*	148.1 ± 1.73*	151.5± 2.69*	143.7 ± 2.66*	131.8± 2.64*	147.9 ± 3.27*	136.1 ± 2.26*

Results are expressed as ± SEM (n=6). * p<0.01 significant when compared to normal group.

REFERENCES

1. King H, Aubert RE, Herman WH. Global burden of diabetes, 1995–2025: prevalence, numerical estimates and projections. Diabetes Care 1998; 21: 1414–1431.
2. World Health Organisation Consultation. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus. Report of a WHO Consultation, Geneva. 1999, pp 14-16.
3. Wild S, Roglic G, Green, A, Sicree R, King H. Global prevalence of diabetes Estimates for the year 2000 and projections for 2030. Diabetes Care 2004; 27: 1047–1053.
4. Rhabasa-Lhoret, R, Chiasson JL. Alpha-Glucosidase inhibitors. In: Defronzo, R.A., Ferrannini, E., Keen, H., Zimmet, P. (Eds.),

International Textbook of Diabetes Mellitus, vol. 1, 3rd ed. John Wiley & Sons Ltd., UK, 2004, pp. 901–914.
5. Bailey CJ. New approaches to the pharmacotherapy of diabetes. In: Pickup, J.C., William, G. (Eds.), Textbook of Diabetes, vol. 2, 3rd ed. Blackwell Science Ltd., UK, 2003, pp. 73.1–73.21.
6. Marles R, Farnsworth N. Plants as sources of antidiabetic agents. In: Wagner, H., Farnsworth, N.R. (Eds.), Economic and Medicinal Plant Research, vol. 6. Academic Press Ltd., UK, 1994, pp. 149–187.
7. Wealth of India, Raw materials, Council of Scientific and Industrial Research New Delhi, Reprinted by the Publication of Information Directorate, New Delhi, 2002, 4 (2), pp 69.
8. Dhanabal SP, Mohan Marugaraja MK, B Suresh. Antidiabetic activity of Clerodendrum phlomidis leaf extract in Alloxan-Induced Diabetic rats. Indian Journal of Pharmaceutical Sciences, 2008; 70 (6): 841-844.
9. Gokani RH, Lahiri SK, Santani DD and. Shah MB. Evaluation of Immunomodulatory Activity of *Clerodendrum phlomidis* and Premna integrifolia Root. Indian Journal of Pharmacololgy, 2007; 3 (4): 352-356.
10. Joshi A, Megeri K. Antiamnesic evaluation of *C. phlomidis* Linn. bark extract in mice. Brazilian Journal of pharmaceutical sciences, 2008; 44(4): 717-725.
11. Kilimozhi D, Parthasarathy V, Amuthavalli N. Effect of *Clerodendrum phlomidis* on adjuvant induced arthritis in rats - A radiographic densitometric analysis. International Journal of PharmTech. Research, 2009; 1(4): 1434-1441.
12. Verma A, Bahar A. Anti-hepatotoxic activity of *Clerodendrum phlomidis*, International Journal of PharmTech. Research, 2009; 1(4): 1028-1031.
13. Rajasekaran A, Ponnusamy K. Antifungal activity of *Clerodendron inerme* (L) and *Clerodendron phlomidis* (L). Turk J Biol, 2006; 30: 139-142.
14. Murugesan T, Saravanan KS, Lakshmi S, Ramya G, Thenmozhi K. Evaluation of psychopharmacological effects of *Clerodendrum phlomidis* Linn. Extract. J Ethanopharmacol, 1999; 68(1-3): 315-319.
15. Rani S, Ahamed N, Rajaram S, Saluja R, Thenmozhi S, Murugesan T. Anti-diarrhoeal evaluation of Clerodendrum phlomidis Linn.leaf extract in rats. J Ethnopharmacol, 1999; 68: 315-319.
16. Seth KK, Pandey VB, Dasgupta B. Flavonoids of *Clerodendrum phlomidis* flowers. Pharmazie, 1982; 37: 74-75.
17. Roy R, Pandey VB. Flavonoids of *Clerodendron phlomidis.* Indian Journal of Natural Product, 1995; 11: 13-14.
18. Anam EM. Novel Flavone and chalcone glycosides from *Clerodendrum* phlomidis (Verbenaceae). Indian Journal of Chemistry, 1997; 36B: 897-900, 1997.
19. Anam EM. Novel Flavone and chalcone glycosides from *Clerodendrum phlomidis* (Verbenaceae). Indian Journal of Chemistry, 1999; 36B: 1307-1310.
20. Dineshkumar B, Mitra A, Manjunatha M. A comparative study of alpha amylase inhibitory activities of common anti-diabetic plants at Kharagpur block. International Journal of Green Pharmacy, 2010; 4:115-21.
21. Hansawasdi C, Kawabata J, Kasai T. α- amylase inhibitors from Roselle (*Hibiscus sabdariffa* Linn.) tea. Bioscience, Biotechnology and Biochemistry, 2000; 64: 1041-3.
22. Kar D, Maharana L, Pattnaik S, Dash G. Studies on hypoglycaemic activity of Solanum xanthocarpum Schrad. & Wendl. fruit extract in rats. J. Ethnopharmacol, 2006; 108: 251–256
23. Kameswara Rao B, Kesavulu MM, Giri R, Appa Rao Ch. Antidiabetic and hypolipidemic effects of *Momordica cymbalaria*, Hook fruit powder in Alloxan diabetic rats. J. Ethanopharmacol, 1999; 67: 103–109.
24. Singleton VL, Rossi JA. Colorimetry of total phenolics with phosphomolybdic-phosphotungstic acid reagents. American Journal of Enology and Viticulture, 1965; 16: 144-158.
25. Liu CT, Ching YW, Yih MW, Chin YT. Ultrasoundassisted extraction methodology as a tool to improve the antioxidant properties of herbal drug Xiao-chia-hu-tang. J Ethnopharmacol, 2005; 99(2): 293-300.
26. Ivorra MD, Paya M, Villar A. A review of Natural Products and Plants as Potent antidiabetic drugs. J Ethnopharmacol, 1989; 27 (3): 243–275.
27. Oliver-Bever, B. Medicinal Plants in Tropical West Africa. Cambridge University Press, London, 1986, pp. 245–267.
28. Atta-Ur-Rhemann, Khurshid Zaman. Medicinal plants with hypoglycemic activity. J Ethnopharmacol, 1989; 26: 1–55.
29. Kameswara Rao B, Giri R, Kesavulu MM. Appa Rao Ch. Herbal medicine: in the management of diabetes mellitus. Manphar Vaidhya Patrika 1997; 1 (4): 33–35.
30. Chakravarthy BK, Gupta S, Gambir SS, Gode KD. Pancreatic beta cell regeneration. A novel antidiabetic mechanism of *Pterocarpus marsupium* Roxb. Indian Journal of Pharmacology, 1980; 12: 123–127.
31. Manickam M, Ramanathan M, Farboodinay Jahromi MA, Chansouria JPN, Ray AB. Antihyperglycemic activity of phenolics from *Pterocarpus marsupium*. Journal of Natural Products, 1997; 60: 609–610.