Journal of Science Research

The aqueous stem bark extract of *Parkia filicoidea* (Fabaceae) possesses anti-diabetic property

[1]Owolabi O. J.*, [1]Nwekwo C. E., [2]Innih S. O.
[1]Department of Pharmacology and Toxicology, Faculty of Pharmacy,
University of Benin, Nigeria.
[2] Department of Anatomy, School of Basic Medical Science, College of Medical Science,
University of Benin, Nigeria.
*Corresponding author E-mail: owolabi@uniben.edu, omonowolabi@yahoo.com, Tel: +2348034120318

Abstract

Parkia filicoidea Oliv (Fabaceae) is a plant indigenous to Nigeria and traditionally used in the treatment of many ailments, one of which is diabetes mellitus. However scientific reports of its folkloric use as anti-diabetic plant are lacking. Therefore, this study is aimed at evaluating the blood glucose lowering effect of *Parkia filicoidea* on streptozotocin induced diabetes in rats. The aqueous stem bark extract was orally administered at 100, 200 and 400 mg/kg doses. Diabetes was induced via an intra-peritoneal administration of streptozotocin 55 mg/kg in wistar albino rats. Glibenclamide (5 mg/kg) a standard reference drug was used as positive control while distilled water (2ml/kg) served as the negative control. An untreated diabetic group was also kept for the period of the experiment. The extract, glibenclamide and distilled water were orally administered daily for 14 days, while the fasting blood glucose level was monitored prior to induction and on days 1, 7 and 14 following induction/treatment. Blood samples were obtained via the abdominal aorta following euthanisation from treated rats on the 14th day and analyzed for glucose and lipid profile. The extract at all doses produced a significant reduction ($p<0.05$) of the fasting blood glucose levels in the diabetic rats from day 1 to 14 compared with the untreated diabetic group. A significant reduction ($p<0.05$) of the total cholesterol and triglycerides level of diabetic rats was observed in the extract treated groups (100, 200 and 400 mg/kg) in comparison with the untreated diabetic group. A significant ($p<0.001$) reduction in the low density lipoprotein was also observed in comparison with the untreated diabetic rats. In conclusion, *Parkia filicoidea* may be a good alternative to orthodox drugs in the management of diabetes mellitus, considering its glucose lowering potentials and positive impact it had on the lipid profile of diabetic rats.

Keywords: Streptozotocin; Diabetes mellitus; Blood glucose; Lipid profile, *Parkia filicoidea*, Rats.

Introduction

The World Health Organization (WHO) estimates that 80% of the populations of some Asian and African countries presently use herbal medicines for some aspect of their primary health care [1]. Many of the pharmaceuticals currently available to physicians have a long history of use as herbal remedies, including opium, aspirin, digitalis and quinine. According to WHO, approximately 25% of modern drugs used in the United States are derived from plants [1].

The use of herbal remedies appears to be more prevalent in patients with chronic disease such as cancer, diabetes, asthma and end-stage renal disease [2]. One of such herbal remedies is *Parkia filicoidea* Oliv (Fabaceae) locally called African locust bean.

Parkia filicoidea is a large spreading flat-crowned tree up to 30 meters tall. African locust bean is used as a food and seasoning for vegetable stews [3]. In Nigeria, the seed which is naturally sweet is processed into a valuable food known as Sikomua and Daddawa among the Yoruba and Hausa people respectively [3].

Although the bark is used in traditional medicine for the treatment of malaria, rheumatism, toothache and diabetes, scientific data on its use in diabetes is scanty. In a survey conducted on healers in Togo and Guinea, *Parkia filicoidea* was one of the highest cited plant used for treating hypertension and malaria respectively [4, 5]. The role of herbal medicine in the treatment of diabetes cannot be overemphasized, maybe because of their effectiveness and lesser risk of side effects when compared with conventional medicines.

Diabetes mellitus (DM), one of the largest global health emergencies of the 21st century [6] is a chronic condition that occurs when there is inadequate amount of insulin or insulin resistance. It results in increased levels of glucose in the blood (hyperglycaemia), with symptoms of polyuria, polydipsia and polyphagia [7].

As at 2015 in Nigeria, about 1.6 million individuals had diabetes and this is estimated to increase by 111 % in the year 2040. The mortality from poorly managed diabetes is huge averaging 112 deaths per day [8]. Orthodox drugs available such as oral hypoglycemic agents, acarbose, thiazolidinediones are all expensive and usually marred with adverse effects hence the need for herbal medicines as substitutes which are devoid of adverse effects, readily available coupled with their affordability.

Parkia filicoidea is used routinely by local herbal healers in treating diabetes mellitus in south-south Nigeria (verbal communication) and there its paucity of scientific data/information of this folkloric use. The plant has not been documented for possible toxicity or adverse effects as studies on the acute/sub-acute toxicity profiles is yet to be investigated.

This study is thus timely and important as it aims to provide a scientific basis for one of the ethnomedicinal use of *Parkia filicoidea*, which is the treatment of diabetes mellitus, this becomes necessary considering the availability, affordability and tolerability of the plant.

Materials and methods

Collection/ Extraction of Plant material

The barks of *Parkia filicoidea* were obtained from Ajaokuta area of Kogi state, Nigeria in May, 2015. It was identified by a taxonomist in the Department of Pharmacognosy, Faculty of Pharmacy, University of Benin and a herbarium specimen exists in the Department. A herbarium specimen was also deposited in the National Institute for Pharmaceutical Research and Development (NIPRID) in Nigeria with this herbarium specimen number: NIPRD/H/6847.

The barks of *Parkia filicoidea* was air-dried and then pulverized into powder sample using a grinder. Two hundred and fifty grams of the powdered plant material was boiled (100 ºC) in 2 L of distilled water in a conical flask for 10 minutes on an electric heater. The boiled extract was allowed to cool and then filtered using cotton wool and the filtrate was passed through Whatmann No. 4 filter paper for further filtration, the filtrate was then concentrated in an oven and then allowed to dry in same oven at a temperature of 40 ºC. The extract was thereafter stored in the refrigerator prior to use and reconstituted with distilled water prior to administration.

Animals

Adult albino rats of either sex weighing between 150-250 g (202 ± 39.6 g) were obtained from the animal house of the Department of Pharmacology and Toxicology, Faculty of Pharmacy, University of Benin, Nigeria. The animals were allowed to acclimatize for 14 days under standard environmental conditions on a regular feed (standard growers mash, Top feeds, Nigeria) and had access to water *ad libitum.*

Ethical approval was obtained from the ethical committee of the Faculty of Pharmacy, University of Benin, Benin City, Edo state, Nigeria and all animals were handled according to the standard protocols for the use of animals in research [9].

Drugs/Chemicals

The following drugs and chemicals were used: Streptozotocin (Sigma-Aldrich, UK), Citrate buffer (Karmel Chemicals) consisting of citric acid and sodium citrate, Glibenclamide (Swiss Pharmaceutical, Nigeria), Chloroform (BDH Chemicals, UK).

Induction of Diabetes Mellitus (DM)

Twenty five adult albino rats were used with 5 animals per group. DM was induced in all rats by administering 55 mg/kg of streptozotocin intraperitoneally to albino rats fasted overnight. Thereafter diabetes was confirmed induced 72 hrs following streptozotocin administration by checking their fasting blood glucose level using a glucometer. Fasting blood glucose levels of rats greater than 200 mg/dL were taken as diabetic. DM status was monitored using blood samples obtained by cutting the tips of the rat tail and checked using a glucometer (Accucheck) [10]. A group consisting of 5 rats was left not treated with streptozotocin and this was the normal control group.

Experimental design

The basal blood glucose level was first ascertained for each animal prior to induction. The diabetic rats were then divided into 5 groups (n= 5).

Group 1 were normal, non-diabetic rats, given distilled water orally, groups 2 to 6 were the diabetic rats; group 2, untreated diabetic rats orally given distilled water (0.2 ml), group 3 was orally given glibenclamide (5 mg/kg; 0.2 ml), groups 4, 5 and 6 were orally given the aqueous extract at 100, 200 and 400 mg/kg doses respectively (0.2ml each). Administration was done orally, daily and for 14 days.

Fasting blood glucose "FBG" level obtained following induction and prior to treatment with extract and glibenclamide was taken as day 0, thereafter FBG was checked on day 1, 7 and 14 following treatment.

Determination of lipid profile

On day 14, two hours following extract and glibenclamide administration, the fasting blood glucose level was first ascertained using a glucometer by cutting the tip of the rats' tail. Thereafter all the animals were sacrificed. This euthanisation was done under chloroform anaesthesia.

Following euthanisation, blood samples were withdrawn via the abdominal aorta following cardiac puncture and transferred into lithium heparin tubes. This was then used for lipid profile analysis (High density lipoprotein, Low density lipoprotein, triglycerides and cholesterol).

Statistical analysis

All data are expressed as mean ± SD. The significance of the differences among the group were assessed using one way ANOVA. The test followed Dunnet's test. P values <0.05 were considered as significant.

Results

Effect on fasting blood glucose level

The result of treatment on the fasting blood glucose level with *Parkia filicoidea* in streptozotocin induced diabetic rats is presented in Table 1. It was observed that the basal blood glucose levels of the rats following induction of diabetes in all the groups (extract, glibenclamide and untreated) were significantly higher ($p<0.05$) than the normal rats. However on day 1 following treatment, a significant reduction ($p<0.05$) was seen in the treated animals as compared to the untreated at all doses. However reduction seen in the group given 200 mg/kg (122.3±57.7 mg/dL) was better compared to 323.3±70.9 mg/dL produced by glibenclamide.

On day 7, ($p<0.05$) significant reduction was produced by all doses with the 100 mg/kg giving the best reduction (211.5±22.5mg/dL) compared to 520.0±38.6 mg/dL of the untreated diabetic. However glibenclamide lowering ability was more effective (157.5±25.33 mg/dL) on this day.

On day 14, significant reduction ($p<0.05$) was produced by all doses in comparison with 568.0±71.6mg/dL of the untreated diabetic group. The 200 mg/kg dose gave the best reduction (145.7±78.3mg/dL) better than that of glibenclamide.

Table 1. The fasting blood glucose of streptozotocin-induced diabetic rats treated with *Parkia filicoidea*

GROUPS (mg/kg)	Pre-induction	Day 0 of induction	Day 1 of induction	Day 7 of induction	Day 14 of induction
Control	60.0 ± 2.10	70.0 ± 2.70	69.0 ± 0.5	70.0 ± 2.1	82.0 ± 1.50
UD	55.9 ±3.85	549.0± 39.2	507.3± 80.3	520.0±38.6	568.0±71.6
DG (5)	52.8 ± 8.23	491.5 ± 75.1	323.3± 70.9*	157.5±25.33*	415.3±61.2
DPF(100)	78.6 ± 4.81	453.2± 12.51	199.0±18.1*[b]	211.5±22.4*	310.0±84.9*
DPF (200)	61.2 ±12.2	553.2 ± 65.9	122.3±57.7[ab]	431.0±67.9	145.7±78.3*
DPF(400)	54.0 ±11.8	500.8±100.8	213.5± 30.4*[b]	263.7±17.0*	427.5±84.1

Values are mean blood glucose levels ± SD in mg/dl.
[*]P<0.05, [a]P<0.001 significantly different from the untreated diabetic group,
[b]P<0.05 significantly different from days 7 and 14.
Control- Normal rats which were not induced.
UD-Untreated diabetic which were induced and given distilled water.
DG (5) -Diabetic rats treated with glibenclamide (5 mg/kg).
DPF (100)-Diabetic rats treated with the 100 mg/kg PF.
DPF (200)-Diabetic rats treated with extract 200 mg/kg PF.
DPF (400)-Diabetic rats treated with extract 400 mg/kg PF.
Extract and glibenclamide were administered daily for 14 days
*Pre-induction precedes Day 0, 1, 7 and 14

Effect on lipid profile

Table 2 shows the effect of treatment using glibenclamide and the different doses of the aqueous extract of *Parkia filicoidea* on the lipid profile of STZ induced diabetic rats.

From the result, in comparison with the negative control, the untreated diabetic rats had significantly ($p<0.001$) higher total cholesterol, triglycerides, high density lipoproteins and low density lipoproteins.

A significant decrease ($p<0.05$) in the triglyceride level less than120 mg/dL was observed in the extract treated diabetics compared to the untreated whose values were above 120 mg/dL, with the 100 mg/kg dose giving the best result of 60.67±7.51 mg/dL.

A significant reduction ($p<0.05$) was also observed in the total cholesterol and LDL in the extract treated groups in comparison with the untreated diabetic rats from 175.4±52.18 mg/dL seen in the untreated to 105.25±22.54 mg/dL, 60.67±7.51 mg/dL, 102.50±31.82 mg/dL and 103.50±10.61 mg/dL for glibenclamide, 100, 200 and 400 mg/kg of the extract respectively.

The LDL level was significantly lowered on treatment by all doses of the extract and glibenclamide. The effect of the extract at 100 and 200 mg/kg showed a significance of $p<0.001$ compared to glibenclamide that was $p<0.05$.

Finally the effect of the extract and glibenclamide on HDL was insignificant compared to the untreated diabetic rats but significantly higher ($p<0.05$) than the control group.

Table 2. The lipid profile of STZ induced diabetic rats treated with the aqueous extract of *Parkia filicoidea*

GROUPS (mg/kg)	TC(mg/dL)	TG(mg/dL)	HDL(mg/dL)	LDL(mg/dL)
Control	42.33± 0.73	42.5 ±2.1	36.08 ±0.26	11.60 ±1.6
Untreated diabetic rats	98.00±39.59	175.40±52.18	55.60±4.15	38.70±3.35
DG (5)	76.00±13.83[a,b]	105.25±22.54[a,b]	50.75±8.30[b]	4.10±16.00[b]
DPF(100)	61.00±14.42[a,b]	60.67±7.51*[b]	49.67±8.33[b]	-0.80±5.74*[b]
DPF (200)	84.33±10.69[b]	102.50±31.82[a,b]	49.33±7.77[b]	0.07±11.44*[b]
DPF(400)	80.00±1.41[a,b]	103.50±10.61[a,b]	52.50±7.78[b]	6.00±9.62[b]

Values are Mean±S.D n= 5 per group.
[a]P<0.05,*P<0.001 significantly different from the untreated diabetic group and
[b]P<0.05 significantly different from the control
TC--- Total cholesterol level
TG--- Triglyceride level
LDL--- Low density lipoprotein level

Discussion

It was observed that there was a significant increase in the blood glucose level of the diabetic rats compared to the basal glucose level of the normal rats. This confirmed the induction of diabetes by streptozotocin [11]. Streptozotocin is a nitrosourea derivative isolated from *Streptomyces achromogenes* possessing broad spectrum antibiotic and antineoplastic activity [12]. It induces Diabetes via selective pancreatic beta cell toxicity and this occurs because its induction is related to the glucose moiety in its chemical structure which enables Streptozotocin to enter the beta cell via the low affinity glucose 2 transporter in the plasma membrane [13]. The β-cells of the pancreas are more active than other cells in their uptake of glucose hence more sensitive than other cells to Streptozotocin challenge. This is supported by the observation that insulin producing cells that do not express this glucose transporter are resistant to Streptozotocin [13].

The results indicate that this plant possess anti-diabetic activity demonstrated by the varying degrees of blood glucose level reduction seen at the different dose levels.

This anti-hyperglycemic action of the extract could be attributed to the presence of tannins, flavonoids and saponins which have been reported to be present in *Parkia filicoidea* in one of our studies yet to be published. Plants with flavonoids, terpenoids, alkaloids and glycosides have anti-oxidant activity and as such possess anti-diabetic effect. Possibly flavonoids reported to be present in the plant may have regenerated the damaged beta cells of pancreas [14, 15], while saponins can inhibit glucose transport by inhibiting sodium glucose co-transporter -1(S-GLUT-1) in the intestine [14; 15].

Glibenclamide, a Sulphonylurea used in this study reduced blood glucose possibly by increasing insulin secretion from pancreatic beta cell. This means they are active in mild streptozotocin-induced diabetes and are inactive in intense streptozotocin-induced diabetes [16]. Different mechanisms of

action of medicinal plants with antidiabetic activity have been extensively described. These include inhibition of renal glucose reabsorption [17], stimulation of insulin secretion from Beta cells of islet of Langerhans or/and inhibition of insulin degradative processes, reduction in insulin resistance [16], regenerating and/or repairing pancreatic beta cells with increasing the size and number of cells in the islets of Langerhans [19].

Lipids play many important roles in the body but can also lead to cardiovascular disease when their concentration is abnormal in an organism, insulin deficiency leads to various metabolic alterations in the animals viz increased blood glucose level and increased cholesterol concentration [20]. Hyperlipidemia is another recognized complication of diabetes mellitus characterized by elevated levels of cholesterol, triacylglycerol and changes in lipoprotein composition.

Most studies have shown that patients with diabetes have more triglyceride and less high-density lipoprotein (HDL) cholesterol than non-diabetics [21]. Our results points to a reduction of the elevated triglycerides level following treatment with *Parkia filicoidea*. A reduction in total cholesterol level and LDL in comparison to both the glibenclamide treated group and the untreated diabetic rats were also observed. These are great advantages for the diabetic individual; hence a dual anti-hyperglycemic and hypolipidemic effect is seen with the extract [22].

Conclusion

In conclusion, the aqueous extract of *Parkia filicoidea* showed significant anti-diabetic activity and was as effective as glibenclamide hence the extract is a good alternative for the treatment of diabetes. The extract also lowered the triglyceride and total cholesterol levels significantly.

This study thus confirms the use of the aqueous extract of *Parkia filicoidea* in diabetes mellitus and further studies on exact mode of action is recommended.

Acknowledgements

Our profound gratitude goes to Mr Ibeh, Mr Stephen Nwele and George Ukioma for their contributions towards this research.

References

[1] Fabricant, D.S. and Farnsworth, N.R. 2001. The value of plants in traditional medicine for drug discovery. *Environ. Health Perspect*, 109 (1)**:** 69-75.

[2] Karl Peltzer, SupaPengpid, ApaPuckpinyo, Siyan Yi, and Le Vu Anh. 2016. The utilization of traditional, complementary and alternative medicine for non-communicable diseases and mental disorders in health care patients in Cambodia, Thailand and Vietnam. *BMC Complement Altern Med*, 16: 92.

[3] Egede, L. E., Zheng, D. and Simpson, K. 2002. Comorbid Depression Is Associated with Increased Health Care Use and Expenditures in Individuals with Diabetes. *Diabetes Care* 25(3): 464–470.

[4] Olaniyan, A. 2013. Locust Bean Products. Non Wood News-No 10. Retrieved November 12,from http://www.fao.org/docrep

[5] Karou, S., Tchacondo, M.D., Abdoul-Rahaman, S., Anani, K., Koudouvo, K. et al 2011. Ethnobotanical study of medicinal plants used in the management of diabetes mellitus and hypertension in the central region of Togo. *Pharm Biol* 49(12):1286-1297.

[6] Trarore, M., Balde, M., Oulare, K., Magassouba, F., Diakite, I., Diallo, A. et al 2013. Ethnobotanical survey on medicinal plants used by Guinean traditional healers in the treatment of malaris. *J Ethnopharmacol*, S0378-8741(13): 773-310.

[7] Tabish, S.A. 2007. Is Diabetes becoming the biggest epidemic of the twenty-first century? Int. J. Health Sci 1(2): v-viii

[8] Alberti KGMM, DeFronzo RA, Zimmet P. International textbook of diabetes mellitus. (2nd ed.). New York: J. Wiley; 1997.

[9] Ogbera, A.O and Ekpebegh C. 2014. Diabetes mellitus in Nigeria, the past, present and future. World J. Diabetes 5 (6): 905-911.

[10] National Institute of Health, USA: 2002. Public Health Service Policy on Humane care and use of Laboratory animals.

[11] Rheney, C.C. and Kirk, K.K. 2000. Performance of the three blood glucose parameters. *Ann Pharmacothera* 34(3): 317-321.

[12] Barnes, P.M., Bloom, B., Nahin, R.L. 2008. Complementary and alternative medicines use among adults and children: United States 2007. National Health Statistic Report 12:1-23

[13] Dolan, M.E. 1997. Inhibition of DNA repair as a means of increasing the antitumor activity of DNA active agents. Adv Drug Del Rev, 26:105– 118.

[14] Elsner M, Guldbakke B, Tiedge M, Munday R, Lenzen S. 2000. Relative importance of transport and alkylation for pancreatic beta-cell toxicity of streptozotocin. Diabetologia 43:1528-1533

[15] Hakkim, F.L., Girija, S., Kumar, R.S. and Jalaludden, M.D. 2007. Effect of aqueous and ethanol extracts of *Cassia auriculata* L. flowers on diabetes using alloxan induced diabetic rats. Int J Diabetes Metab 15:100-106.

[16] Tiwari, A.K. and Rao, J.M. 2002. Diabetes mellitus and multiple therapeutic approaches of Phytochemicals: Present status and future prospects. *CurrSci* 83:30-38.

[17] Yalow, R.S. 1980. Radioimmunoassay. *Ann Rev BiophysBiven* 9:327-345

[18] Eddouks, M., Maghrani, M., Lemhadri, A., Ouhidi, M.L and Jouad, H. 2002. Ethnopharmacological survey of medicinal plants used for the treatment of diabetes mellitus, hypertension and cardiac diseases in the south-east region of Morocco. *J of Ethnopharmacol* 82:97-103.

[19] Pulok, K.M., Kintal, M., Kakali, M. and Peter, J.H. Leads from Indian medicinal plants with hypoglycemic potentials. *J. Ethnopharmacol* 106:1

[20] Mohamed, B., Abderrahim, Z., Hassane, M., Abdelhafid, T. and Abdelkhaleq, L. 2006. Medicinal plants with potential antidiabetic activity.-A review of ten years of herbal medicine research. *Intl J Diab Meta* 14:1-25

[21] Murugan, M. and Reddy, C.U.M. 2009. Hypoglycemic and hypolipidemic activity of leaves of *Mucuna pruriens* in alloxan induced diabetic rats. *J Pharm Sci Tech* 1(2): 69-73.

[22] Ginsberg, H.N. 1991. Lipoprotein physiology in non-diabetic and diabetic states. Relationship to atherogenesis. *Diab Care* 14: 839-855.

[23] Syvanne, M. and Taskinen, M.R. 1997. Lipids and lipoproteins as coronary risk factors in non-insulin dependent diabetes mellitus. *Lancet* 350(1):120-123.

Journal of Science Research ISSN 1119 7333
Citation: Owolabi O.J., Nwekwo C.E. and Innih S.O.
The Aqueous stem bark extract of *Parkia filicoidea (*Fabaceae*)*possesses anti-diabetic property Volume 17, 2018, pp 1-6