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ABSTRACT

Background: Diabetes mellitus is a global health problem leading to an increase in the search for herbal normoglycaemic agents as alternative to the synthetic ones. Aqueous extract of *Parkia biglobosa* leaves was assessed for normoglycaemic effects in alloxan-induced diabetic rats. The study aim at providing scientific evidence to authenticate the traditional use of *Parkia biglobosa* leaves in the treatment of diabetes.

Methodology: The plant was extracted using aqueous to obtain *Parkia biglobosa* Leaf Extract (PbLE), qualitative phytochemical analysis was determined using standard methods. Diabetes was induced in albino rats by intraperitoneal injection of 5% solution of alloxan (150 mg/kg bw). The rats were grouped into 5 groups (A, B, C, D and E) of 5 animals each. Group A consisted of non-diabetic rats which served as the control, Group B consisted of diabetic rats that were left untreated and served as negative control, Group C were given glucophage (reference) at a dose level of 7 mg/kg bw, Groups D and E were administered PbLE at the doses of 250 and 500 mg/kg bw respectively.

Results: The glucose levels in the blood of rats were checked with a glucometer using the blood from the tail of the rats. Serum (proteins, lipid profiles, urea and creatinine), ALT, AST and ALP were all determined using standard procedures. The extract and the glucophage reduced the blood glucose level significantly ($p < 0.05$) from day 3 till the termination of the experiment.

Conclusion: Aqueous extract of *Parkia biglobosa* leaves possess antidiabetic activity and also the extract is relatively safe. Hence the leaves of *Parkia biglobosa* can be explored in producing alternative antidiabetic drugs.

Key words: alloxan, diabetic mellitus, glucophage, normoglycaemic, *Parkia biglobosa*

Introduction

Medicinal plants have made the basis of health care throughout the world since the earliest days of humanity and are still widely used and have significant importance in international trade (Ahmad *et al.*, 2006 Abubakar *et al.*, 2019). In some African countries for instance, up to 90 percent of the population still rely absolutely on plants as a source of medicines (Hostettmann, *et al.*, 2000). In Nigeria, about 85 percent of the population patronise traditional medicine practitioners for their health care; in spite of this high patronage, the products and practices of traditional medicine are still highly misunderstood (NNMDA, 2005).. Medicinal plant refers to any part, tissue or organ of a plant species containing substances usable for therapeutic purposes, or which serve as precursors for the synthesis of more useful drugs with minimal side effects (WHO, 1980). Diabetes mellitus is a serious metabolic disorder with micro and macro vascular complications that results in significant morbidity and mortality (Rang *et al.*, 1991). Chronic hyperglycaemia during diabetes causes glycation of body protein that in turn leads to secondary complications affecting the eyes, kidney, nerves and artery (Sharma, 1993). These effects may be delayed, lessened or prevented by maintaining blood glucose values close to normal. The increasing number of ageing population, consumption of calorie rich diet, obesity and sedentary life style have led to a tremendous increase in number of diabetes worldwide (Sharma, 1993). According to World Health Organization projection, the prevalence of diabetes is likely to increase by 35 percent. Currently there are over 150 million diabetics worldwide and this is likely to increase to 300 million or more by the year 2025. Statistical projection about India suggests that the number of diabetics will rise from 15 million in 1995 to 57 million in the year 2025 making India the country with the highest number of diabetics in the world (Boyle *et al.*, 2001). *Parkia biglobosa* (family- mimosaceae) is known as the African locust bean tree (English), as *Igba* or *Irugba*, (Yoruba), as *Dorowa* (Hausa) and in Igbo as Origili. (Daziell, 1937). *Parkia biglobosa* is found commonly everywhere in the savannah and it grows up to about 20m high (Ajaiyeoba, 2002). The pinnae of *Parkia biglobosa* are about 6-11 pairs and the leaflets occur in 14-30 pairs (Andrew, 1956). The fermented seeds of *Parkia biglobosa* are used in all parts of Nigeria and indeed the West Coast of Africa for seasoning traditional soups (Aiyelaagbe *et al.*, 1996). *Parkia* species have found use traditionally as food, medicinal agents and are of high commercial value. It is known to provide an ingredient that is used in leprosy, and for treating hypertension (Aiyelaagbe *et al.*, 1996). In Gambia, the leaves and roots are used in preparing a lotion for eyesores, a decoction of the bark of *Parkia biglobosa* is also used as a bath for fever, and the pulped bark is used along with lemon for wound and ulcer (Irvine, 1961).

For a complex disease like diabetes mellitus, little is talked about in the aspects of prevention and cure, rather more emphasis is laid on the management. It is therefore necessary to look for an urgent solution to manage diabetes mellitus. There is an increased focus on plants in the search for appropriate hypoglycaemic or antidiabetic agents. Ethno botanical information showed that more than 800 plants are used as traditional remedies for the treatment of diabetes due to their effectiveness, less side effects and relatively low cost (Ghada, 2013). The available oral hypoglycaemic agents are associated with side effects which include hypoglycaemia, weight gain, gastrointestinal disorders, peripheral oedema and impaired liver function, as well as high cost of treatment (Abubakar, 2019). Natural remedies are one way or another safer and more efficient than pharmaceutically derived remedies, the practice or study of medicinal herbs has become mainstream worldwide (Joseph and Jini, 2013).

Materials and methods

Plant material

Fresh leaves of *Parkia biglobosa* were obtained from University of Ilorin Main Campus, Ilorin South Local Government Area, Kwara State, Nigeria in July 2015. The authentication of the plants was done at the Plant Biology Department of the University of Ilorin, Ilorin Kwara state, Nigeria. A voucher specimen was deposited at the Herbarium of the Department and a voucher number was issued

Experimental Animals

Female Wistar rats weighing between 180-200 g were used for the study. The animals were obtained from the Animals Holding Unit of the Department of Biochemistry, University of Ilorin. They were housed in plastic cages at room temperature and were allowed to acclimatise for one week; with free access to water and normal rat pellet *ad libitum*. Ethical clearance for the study was obtained from the University of Ilorin Ethical Review Committee where ethical number was issued.

Chemicals and Reagents

Assay kits for alanine transaminase, aspartate transaminase, alkaline phosphatase (ALP), total protein, albumin, cholesterol, triglycerides, high-density lipoprotein, and low-density lipoprotein were obtained from Randox laboratories limited, Antrim, United Kingdom. Alloxan monohydrate was obtained from Sigma Chemical Company, St Louis MO, U.S.A. Accu-chek active (glucometer) and the strips were obtained from Roche diagnostics GmbH., Mannheim, Germany. All other reagents used were of analytical grade and were prepared in volumetric flask using all glass distilled water unless otherwise stated.

Preparation of the Plant Extract

Fresh leaves of *Parkia biglobosa* were rinsed twice with tap water and then dried at room temperature for 7 days. The dried leaves were then grounded into powder using an electric blender. The dried powder of the plant (250 g) was then extracted in 1000 ml distilled water for 48 hours. The extract was filtered through Whatman No. 1 filter paper. The resulting filtrate was then evaporated under reduced pressure using a rotary evaporator at 40°C to give a percentage yield of $22.55 \pm 4.25\%$ (w/w) *Parkia biglobosa* Leaf extract (PbLE). The residue was then reconstituted in distilled water to give the required doses used.

Phytochemical Screening

Leaf extract of *Parkia biglobosa* was evaluated for preliminary screening of secondary phytochemicals, alkaloids and saponins were determined following the method described by Harbone (1973), flavonoids, Diterpenes, Tannins, Steroids and Terpenoids were determined using the procedure describe by Odebisi and Sofowora (1978). Glycosides, were determined using the procedure described by (Trease and Evans 1985). All the determination were done with slight modification.

Laboratory Animal

The animals were grouped after induction of diabetes randomly into five (A, B, C, D and E). Animals in Group A which was the control group that were not induced with diabetes were orally administered with 1 ml of distilled water on daily basis for 11 days, animals in group B that was the diabetic untreated group were administered with distilled water throughout the period of the experiment. Group C animals were administered orally glucophage on daily basis for 11 days. Groups D and E were orally administered with the extract of *Parkia biglobosa* on dosage of 250 mg/kg and 500 mg/kg respectively on daily basis for 11 days.

Induction of Diabetes

Diabetes mellitus was induced in the animals by single intraperitoneal dose of 150mg/kg body weight of alloxan. On the third day of induction, the animals were fasted for 6 hours and blood was taken from the tail of the rats to confirm diabetes (Burecelin *et al.*, 1995).

Determination of blood glucose level

All blood samples were collected from the tail of the rats. The blood glucose levels were determined using Accu-chek active glucometer.

Biochemical Analysis

Alanine and Aspartate amino transferase were determined using the method of Reitman and Frankel (1957), alkaline phosphatase was determined using the method of Akanji and Ngaha (1989). Total protein concentration in the serum was determined, using Biuret reagent as described by Gornall *et al.* (1949). The procedure described by Dumas *et al.* (1971) was used for the determination of serum albumin. Bilirubin concentration was determined using the procedure described (Dumas *et al.*, 1985). Concentration of urea and creatinine was determined as described by Tietz *et al.* (1995). Concentration of total cholesterol in the serum was determined using the procedure described by Fredrickson *et al.* (1967). Triacylglycerol and high density lipoprotein cholesterol were determined using the method described by Tietz (1990) and Tietz (1976) respectively.

Statistical Analysis

All results were expressed as mean \pm Standard Error of Mean (SEM). One-way analysis of variance (ANOVA) using graph pad prism (version 7) followed by Tukey's Multiple Comparisons Test to analyse differences among different mean, differences were considered statistically significant at $p < 0.05$.

Results

Secondary Metabolites Detected in *Parkia biglobosa* Leaf Extract

The secondary metabolites detected in aqueous extract of *Parkia biglobosa* leaves are presented in Table 1. The extract was found to contain 6 secondary metabolites namely: alkaloids, saponins, tannins, phenols, flavonoids and glycosides.

Table 1: Secondary Metabolites Detected in *Parkia biglobosa* Leaf Extract

Constituents	Results
Alkaloids	detected
Tannins	detected
Glycosides	detected
Saponins	detected
Steroids	not detected
Flavonoids	detected
phenols	detected
Diterpenes	not detected
Terpenes	not detected

Blood Glucose Levels of Normal and Alloxan-induced Diabetic Rats Treated with PbLE for 11 Days

Blood glucose levels of normal and alloxan-induced diabetic rats are shown in table 2. Extract administration at both 250 and 500 mg/kg bw significantly ($p < 0.05$) lowered blood glucose levels from the initial level up to day eleven of extract administration. The glucose levels of the two test groups became comparable ($p < 0.05$) with control after day 7 of extract administration. Glucose levels of control do not increase significantly ($p < 0.05$) throughout the period of administration. Glucose level of diabetic-untreated continues to increase significantly ($p < 0.05$) throughout the period of the administration. Glucose levels of glucophage group continues to decrease significantly ($p < 0.05$) throughout the period of administration and was comparable to the control after day 3 of administration. The glucose levels of extract treated groups (250 and 500 mg/kg bw) were comparable with glucophage group after day 7 of administration.

Table 2: Blood Glucose Levels of Normal and Alloxan-induced Diabetic Rats Treated with PbLE for 11 Days

Day	Control	Diabetic Untreated	Glucophage	250 mg/kg bw	500 mg/kg bw
0	82.5 ± 3.29 ^a	81.0 ± 1.60 ^a	83.3 ± 0.09 ^a	84.3 ± 2.8 ^a	84.0 ± 2.79 ^a
1	87.5 ± 4.29 ^a	261.0 ± 7.60 ^b	273.3 ± 1.09 ^c	334.3 ± 8.80 ^d	314.0 ± 4.79 ^e
3	82.7 ± 1.76 ^a	297.7 ± 9.33 ^b	222.0 ± 1.15 ^c	315.8 ± 5.20 ^d	244.0 ± 4.59 ^e
5	89.6 ± 5.40 ^a	273.0 ± 2.86 ^b	183.3 ± 5.93 ^c	143.8 ± 8.21 ^d	148.0 ± 2.03 ^d
7	87.0 ± 1.73 ^a	345.0 ± 2.16 ^b	84.3 ± 2.33 ^a	106.0 ± 8.72 ^c	95.3 ± 1.49 ^d
9	79.5 ± 0.50 ^a	358.0 ± 17.04 ^b	78.3 ± 4.91 ^a	84.3 ± 5.78 ^a	80.7 ± 1.24 ^a
11	82.0 ± 1.61 ^a	359.3 ± 2.35 ^b	84.3 ± 4.80 ^a	84.0 ± 3.61 ^a	77.0 ± 2.52 ^a

Values are mean ± SEM of five replicates; Values with different superscripts across the rows are significantly different ($p < 0.05$).

Serum Lipid Profiles of Normal Alloxan-induced Diabetic Rats Treated with PbLE for 11 Days

Serum Lipid Profiles of Alloxan-induced Diabetic Rats Treated with PbLE is shown in Table 3. There was no significant ($p < 0.05$) change in HDL-C concentration in animals of 250 and 500 mg/kg groups when compared to control. Significant ($p < 0.05$) increase in total cholesterol and triglycerides was observed in diabetic-untreated, glucophage, 250 and 500 mg/kg groups when compared to the control. Significantly ($p < 0.05$) reduction in LDL-C concentration was observed in animals of 500 mg/kg group, significant ($p < 0.05$) increase in LDL-C concentration was observed in animals of diabetic untreated group when compared to control.

Table 3: Serum Lipid Profiles of Normal Alloxan-induced Diabetic Rats Treated with PbLE for 11 Days

Serum lipids (mg/100 ml)	Control	Diabetic untreated	Glucophag e	250 mg/kg	500 mg/kg
HDL-C	10.90 ± 0.06 ^a	2.30 ± 0.15 ^b	10.88 ± 0.09 ^a	11.03 ± 0.09 ^a	10.81 ± 0.05 ^a
LDL-C	2.16 ± 0.01 ^a	5.34 ± 0.11 ^b	2.19 ± 0.04 ^a	2.19 ± 0.07 ^a	2.25 ± 0.11 ^a
Total Cholesterol	15.13 ± 0.05 ^a	15.64 ± 0.21 ^b	14.57 ± 0.08 ^a	16.70 ± 0.21 ^a	15.43 ± 0.02 ^a
Triglyceride s	2.19 ± 0.01 ^a	9.20 ± 0.02 ^b	2.30 ± 0.01 ^a	2.26 ± 0.01 ^a	2.36 ± 0.01 ^a

Values are mean ± SEM of five replicates; Values with different superscripts across the rows are significantly different ($p < 0.05$).

Percentage Organ to Body Weight Ratio of NoAlloxan-induced Diabetic Rats Treated with PbLE for 11 Days

Percentage Organ to Body Weight Ratio of Alloxan-induced Diabetic Rats Treated with PbLE is shown in Table 4. There was no significant ($p < 0.05$) change in organ to body weight ratio in both the liver and kidney for animals administered glucophage and 250 mg/kg bw when compared to control. Significant ($p < 0.05$) decrease in liver to body weight was observed in diabetic-untreated animals and in 500 mg/kg bw PbLE when compared to control, glucophage and 250 mg/kg bw PbLE.

Table 4: Percentage Organ to Body Weight Ratio of Normal and Alloxan-induced Diabetic Rats Treated with PbLE for 11 Days

Organ	Control	Diabetic untreated	Glucophage	250 mg/kg	300 mg/kg
Liver	4.10 ± 0.01 ^a	2.00 ± 0.01 ^b	4.00 ± 0.01 ^a	4.00 ± 0.03 ^a	5.00 ± 0.02 ^c
Kidney	1.00 ± 0.01 ^a	1.00 ± 0.02 ^a	1.00 ± 0.01 ^a	0.9 ± 0.01 ^a	1.00 ± 0.01 ^a

Values are means ± SEM of five replicates; values with different superscripts down the column indicates significance at $p < 0.05$

Alanine Aminotransferase (ALT) Activity of Normal and Alloxan-induced Diabetic Rats Treated with PbLE for 11 Days

Alanine Aminotransferase activity of normal alloxan-induced diabetic rats treated with PbLE is depicted in Figure 1. Significant ($p < 0.05$) increase in serum ALT activity with corresponding decrease in ALT activity of the liver was observed in diabetic-untreated animals when compared with the control, however there was no significant change ($p < 0.05$) in serum and liver ALT activity of animals administered with glucophage, 250 and 500 mg/kg bw PbLE when compared with the control. There was no significant ($p < 0.05$) change in ALT activity of the kidney in animals administered glucophage, 250 and 500 mg/kg bw PbLE when compared with the control, however there was significant ($p < 0.05$) increase in kidney ALT activity of diabetic-untreated group when compared with the control.

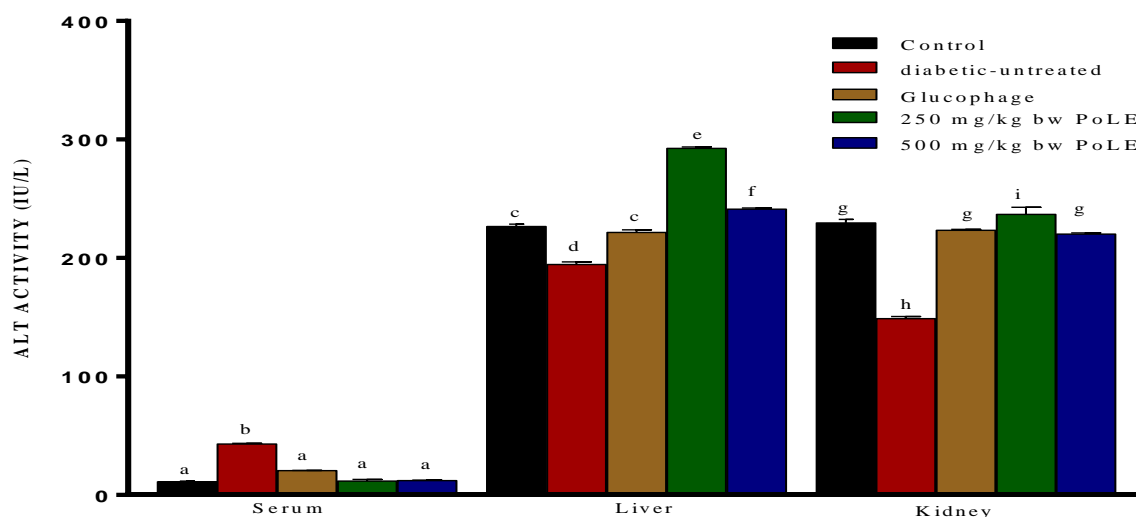


Figure 1: Alanine Aminotransferase Activity of Alloxan-induced Diabetic Rats Treated with PbLE for 11 Days

Aspartate Aminotransferase Activity of Normal and Alloxan-induced Diabetic Rats Treated with PbLE for 11 Days

Aspartate aminotransferase activity of alloxan-induced diabetic rats treated with PbLE is depicted in Figure 2. Significant ($p < 0.05$) increase in AST activity of the liver was observed in diabetic-untreated, glucophage, 250 and 500 mg/kg groups when compared to the control. There was no significant ($p < 0.05$) change in AST activity of the kidney in animals' of 250 mg/kg and in glucophage groups when compared to the control. There was significant ($p < 0.05$) increase AST activity in animals of 500 mg/kg and diabetic untreated groups when compared to control. There was no significant ($p < 0.05$) change in serum activity of the enzyme in animals in all the groups.

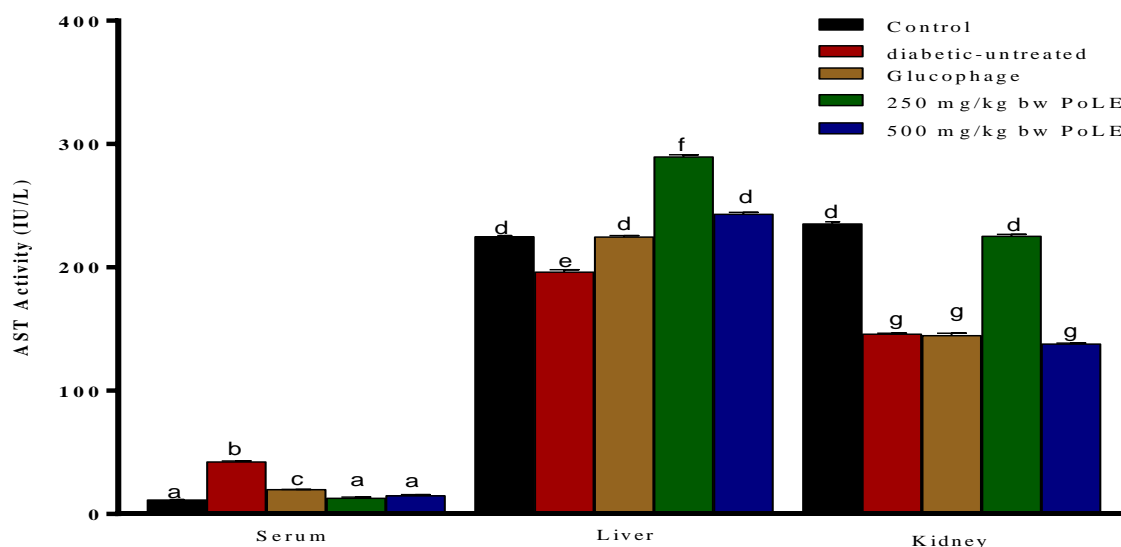


Figure 2: Aspartate Aminotransferase Activity of Alloxan-induced Diabetic Rats Treated with PbLE for 11 Days

Alkaline Phosphatase Activity of Alloxan-induced Diabetic Rats Treated with PbLE for 11 Days

The effect of administration of aqueous extract of *Parkia biglobosa* leaves on ALP activity of liver, kidney and serum of alloxan-induced diabetic rats is depicted in Table 22. Significant increase ($p < 0.05$) in ALP activity of the liver was observed in animals of diabetic untreated group, significant reduction ($p < 0.05$) in ALP activity of the liver was observed in animals of glucophage and 500 mg/kg body weight groups when compared to the control. There was no significant change in ALP activity of the liver in animals of 250 mg/kg body when compared to the control.

Significant increase ($p < 0.05$) in ALP activity of the kidney was observed in animals of diabetic untreated, glucophage 250 and 500 mg/kg groups when compared to the control. There was significant increase ($p < 0.05$) in serum ALP activity in animals of all the tested groups when compared to control.

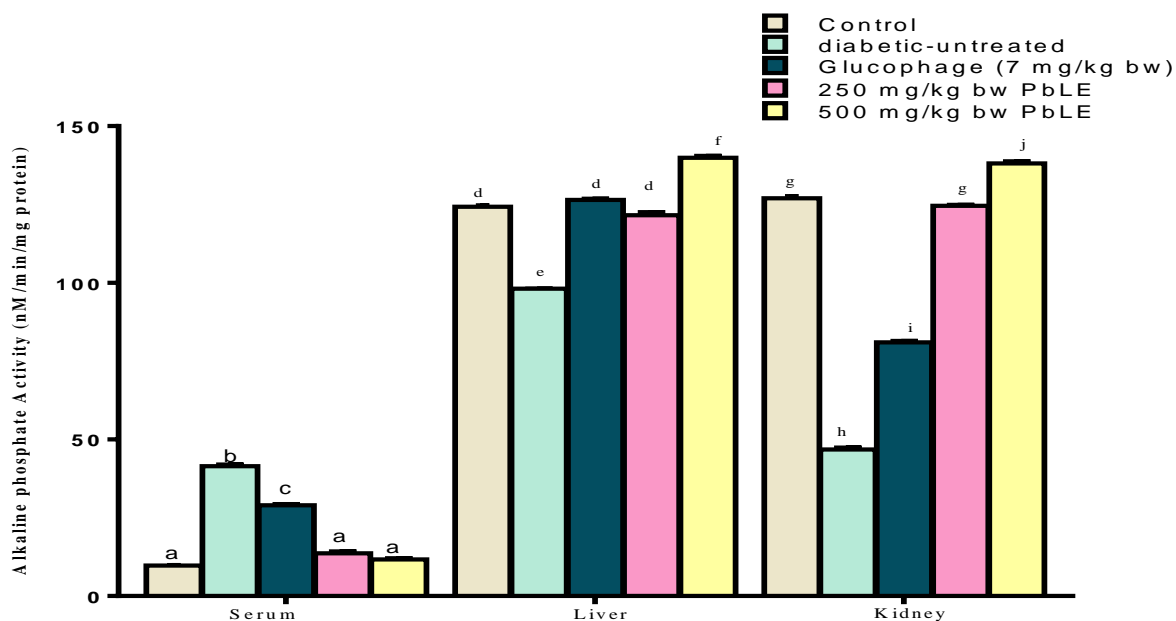


Figure 3: Alkaline Phosphatase Activity of Alloxan-induced Diabetic Rats Treated with PbLE for 11 Days

Values are means \pm SEM of five replicates; bar values with different superscripts indicates significance at $p < 0.05$; PbLE= *P. biglobosa* Leaf extract

Effect of administration of aqueous extract of *Parkia biglobosa* leaves on Liver and Kidney Function Indices

The effect of administration of aqueous extract of *Parkia biglobosa* leaves on serum protein, albumin, urea and creatinine concentration is shown in Table 19. There was no significant change ($p > 0.05$) in serum protein, albumin, urea and creatinine concentration of animals in 250 and 500 mg/kg groups as well as in glucophage group when compared to control, however in diabetic untreated group there was significant change ($p < 0.05$) in the concentration of all the parameters mentioned earlier when compared to control.

Table 5: Effect of administration of aqueous extract of *Parkia biglobosa* leaves on Liver and Kidney Function Indices

parameters	Control	Diabetic untreated	Glucophag e	250 mg/kg	500 mg/kg
Protein (g/dl)	37.2 ± 1.1 ^a	10.4 ± 2.4 ^b	27.1 ± 1.8 ^c	36.9 ± 2.5 ^a	37.0 ± 1.9 ^a
Albumin (g/dl)	21.4 ± 0.5 ^a	11.1 ± 0.7 ^b	16.4 ± 1.6 ^c	22.2 ± 1.7 ^a	21.5 ± 0.4 ^a
Bilirubin (g/dl)	2.4 ± 1.5 ^a	11.1 ± 0.7 ^b	8.4 ± 0.2 ^c	2.2 ± 0.2 ^a	2.5 ± 0.2 ^a
Creatinine (mmol/l)	38.5 ± 0.7 ^a	79.3 ± 2.2 ^b	18.2 ± 7.6 ^c	38.2 ± 1.0 ^a	37.9 ± 1.3 ^a
Urea (mmol/l)	2.0 ± 0.2 ^a	7.8 ± 0.2 ^b	2.1 ± 0.3 ^a	2.5 ± 0.4 ^a	2.7 ± 0.4 ^a
Uric acid (mmol/l)	4.0 ± 0.1 ^a	8.5 ± 0.4 ^b	2.5 ± 0.3 ^a	4.2 ± 0.1 ^a	4.5 ± 0.3 ^a

Values are means ± SEM of five replicates; values with different superscripts across the rows indicates significance at $p < 0.05$; PbLE= *P. biglobosa* Leaf extract

Discussion

Man has been dependent on plants for his food and medicine for relief from illness from the time immemorial, (Christopherson *et al.*, 1991). Plants owe their value as drugs to the medicinal properties of specific inorganic and organic chemical entities present within.

The presence of Saponins, alkaloids and glycosides in *Parkia biglobosa* contributes to its medicinal values. The hypoglycaemic property of *P. biglobosa* may be attributed to the presence of these bioactive compound. These compounds have been shown to be responsible for hypoglycaemic activity in some medicinal plants (Islam, 2011; Joseph, 2011). Alloxan monohydrate is a diabetogenic agent that is widely used in experimental animals to induce diabetes (Bailey and Bailey, 1947). This action is mediated by beta cell destruction, which results in an insulin-dependent syndrome characterised by severe hyperglycaemic, polydipsia, glucosuria and loss of weight (Ahktar *et al.*, 1981). The Observed hyperglycemia in diabetic rats following alloxan induction might also be due to induced gluconeogenesis in the absence of insulin (Yao *et al.*, 2006). Diabetes mellitus is a serious chronic disorder (Zhou, 2009). It is characterised by high blood glucose level due to absolute and relative lack of insulin (Villasenor *et al.*, 2006). Traditional medicinal plants are used throughout the world for the treatment of wide range of diabetic complications. Plants extracts like *Parkia biglobosa* that are used as anti-diabetics contain one or

more bioactive constituents suggesting that the bioactive constituents could act separately or synergistically to produce normoglycaemic effects (Marles and Farnsworth, 1995).

In this study, *Parkia biglobosa* leaf extract reduced hyperglycemia after 6 days of oral administration. The lowering of blood glucose levels due to the administration of *P. biglobosa* leaf extract confirmed the claim of the use of different parts of *P. biglobosa* in traditional medicine for treatment of diabetes (Ukpanukpong *et al.*, 2017). There might be more than one mechanism for the antihyperglycaemic effects of *p. biglobosa* leaf extract. One of the possible mechanisms by which the extract causes normoglycemic condition might probably be due to increasing the insulin effects of plasma by stimulating insulin release from the pancreatic β -cells. (Mahmod and Ojewola, 2003). Beside this, other mechanism might include the stimulation of peripheral glucose utilisation or enhancing glycolytic and glycogenic processes with concomitant decrease in glycogenolysis and gluconeogenesis (Andrade-Cetto and Wiedenfeld, 2004).

The unusually high concentration of serum lipids in diabetes mellitus is mostly due to an increase in free fatty acids from the peripheral fat depots, since insulin inhibits the hormone sensitive lipase. The marked hyperlipidaemia that characterises the diabetic state could therefore be regarded as a consequence of the uninhibited actions of lipolytic hormones on the fat depots (Zahid *et al.*, 2012). The lipid profile obtained in the present study showed a significant decrease in total cholesterol, low density lipoprotein cholesterol and triglycerides in extract treated groups when compared with diabetic-untreated group. The observed increase in serum lipids of diabetic-untreated animals is in agreement with the reports of Fernandes *et al.* (2010), who established that increased in serum lipids was as a result of diabetes in animals.

The hepatic serum enzymes are valued tool in clinical diagnosis that provides information on the effect and nature of pathological damage to any tissue (Daisy and Saipriya, 2012). Alanine aminotransferase, aspartate aminotransferase and alkaline phosphatase are biomarkers which are frequently used for assessment of the integrity of the plasma membrane and tissues after being exposed to pharmacological agents like plant extracts (Giboney, 2005). Result obtained in the present study revealed that the activities of serum liver enzymes; alanine aminotransferase, aspartate aminotransferase and alkaline phosphatase of animals treated with the extract, were significantly increased when compared with the non-diabetic control but with a decrease when compared to diabetic control. ALT was significantly decreased in the extract treated diabetes group compared to the control. This report is consistent with the studies of Abolfathi *et al.* (2012) who reported that the elevation in markers of liver injury such as ALT, AST and ALP indicated hepatocyte damage in experimental diabetes. And the increase in the level of these enzymes in diabetes may be as a result of leaking out of these enzymes from the compromised tissue into the blood stream (Akanji *et al.*, 1993). The ability of *Parkia biglobosa* leaf extract to ameliorate diabetic condition in animals with significantly decrease the ALT, AST and ALP serum levels suggest their hepato-cellular protective function and this can be attributed to the presence of tannins and flavonoids that have been reported to possess antioxidant effects.

Changes in organ to body-weight ratio as suggested by Moore and Dalley (1999) may be an indication of cell constriction or inflammation since the cells are the unit components of organs. Constriction in the organ may occur as a result of loss of fluid from the organ due to damage, while increase in organ-body weight ratio may suggest inflammation. The fact that no significant change was observed in the liver to body weight ratio and the kidney to body weight ratio of diabetic

animals treated with the extract suggested that administration of PbLE might not have resulted into constriction or inflammation of the cells.

Total protein, globulin and albumin are markers of liver biosynthetic ability (Owen *et al.*, 2011). Proteins are synthesised in response to environmental insults from exogenous or endogenous substances, thereby, adapting the cells to fight back. Thus proteins are synthesised to protect the cells, tissue and organs and to rebuild worn out ones (Josiah *et al.*, 2012). Albumin is the major osmolar component of the blood serum and is produced by the liver (Singh *et al.*, 2011). Albumins are proteins that maintain the isotonic environment of the blood so that cells of the body do not gain or lose water in the presence of body fluids. Albumin is the most abundant protein in human plasma, representing 55-65% of the total protein (Josiah *et al.*, 2012). It is synthesised in the liver at a rate that is dependent on protein intake subject to feedback regulation by the plasma albumin level (Al-Hashem *et al.*, 2009). No significant ($p < 0.05$) difference was observed in total protein and albumin of diabetics' rats treated with PbLE when compared with the control; this implies that the extract was able to reverse the toxicity imposed on the organs as a result of diabetes. Significant ($p < 0.05$) decrease in total protein and albumin that was observed in diabetic-untreated rats is an indication of damage to the liver as a result of diabetes

Bilirubin is the yellow breakdown of normal haem catabolism. It is excreted in bile and urine. Bilirubin can be conjugated with a molecule of glucuronic acid, which makes it soluble in water, thereby, facilitating its excretion into bile (Singh *et al.*, 2011). Bilirubin is a marker for hepatobiliary disease and a useful test to substantiate the functional integrity of the liver. Serum bilirubin is considered a true test of liver function as it reflects the liver's ability to take up process and secrete bilirubin into the bile. Elevation in serum bilirubin indicates liver damage. Normally, small amount of bilirubin circulates in the blood (Rosen and Keefe, 1998). Alteration in the concentration of total protein, albumin and bilirubin may indicate the state of the liver and type of damage (Yakubu *et al.*, 2005). Low level of albumin and high level of bilirubin in the serum is an indication of impairment of liver biosynthetic function (Dahiru and Obioda, 2008). No significant difference was observed in total protein, bilirubin and albumin of diabetic-rats treated with PbLE when compared with the control; this is an indication that the secretory functions of the liver were not impaired by the extract.

Creatinine, urea and uric acid are kidney function parameter. Analysis of creatinine in serum is an important clinical test for renal disease and dysfunction. Creatinine is removed from plasma by the glomerulus and then excreted in the urine. Serum creatinine concentration is related to muscle mass. Increased serum creatinine is associated with decrease in glomerular filtration rate. However, serum creatinine levels do not rise until renal function has decreased by at least 50%. Independent of diet, serum creatinine concentration depends upon its excretion rate from the kidneys (Wyss and Kaddurah-Daouk, 2000). Under normal physiologic conditions, urea is the primary vehicle for the excretion of metabolic nitrogen. Urea is a low threshold substance, this is why it is rapidly cleared from vascular system by the renal system. Raised level of serum urea concentration is diagnostic of renal dysfunction (Ibegbulem *et al.*, 2015). Administration of CPLE to normal rats resulted into non-significant difference in creatinine and urea concentrations when compared with the control. This is an indication that the function of the kidney is not compromised by the extract.

Conclusion

- This study revealed that the aqueous extract from *Parkia biglobosa* at the dose levels used, exhibits hypoglycemic activity, its efficacy in managing insulin dependent diabetes offers promising perspective, which deserves further investigation.
- It was shown in this study that Saponins, glycosides, alkaloids, flavonoids and tannins are present in the extract, these bioactive compounds may contribute to the hypoglycaemic activity exhibited by the extract, further studies is needed to clarify the details.

Recommendations

- The leaves of *Parkia biglobosa* can be explored in producing alternative antidiabetic drugs.
- Further study is required to know the bioactive compound that are actually responsible for the antidiabetic effects of *Parkia biglobosa* leaves extract.
- The study can be explored further to know the mechanism of action of the bioactive constituents.

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