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HYPOGLYCEMIC AND HYPOLIPIDEMIC EFFECT OF STEM BARK EXTRACT OF *Kigelia Africana* (SAUSAGE TREE) ON ALLOXAN INDUCED DIABETIC EXPERIMENTAL RATS.

Said Sani Said[1]*, Abdullahi Muhammad Abdu[1] and Aminu Sabo Abdullahi[2]

[1]Department of Biochemistry and Molecular Biology, Federal University Dutsinma Katsina, Nigeria.
[2]Jigawa State Ministry of Education.

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***Corresponding Author**
Said Sani Said
Department of Biochemistry and Molecular Biology, Federal University Dutsinma Katsina, Nigeria.

ABSTRACT

Diabetes mellitus (DM) is a serious endocrine disorder either as a result of insulin resistance or insulin action. While the former is termed type I DM, the latter is referred to as type II DM. The aim of this study is to investigate the effect of methanolic stem bark extract of *Kigelia africana* (SBEka) on alloxan-induced diabetic rats. The extract was screened for phytochemical and antidiabetic properties. Alkaloids, Flavonoids, Anthraquinones, Saponins and Steroids were present in high amount. Tannins and Cardiac glycosides were present in moderate amount, while Volatile oils were totally absent. Diabetes was induced in rats after 18 hours of fasting intraperitoneally by alloxan (100 mg/kg). A total of 25 rats used, the rats were divided into five groups (GI-GV) of five rats each. GII-GV was induced with diabetes. GI served as normal control, GII were administered only distilled water and GIII were administered the standard anti-diabetic drug Glibenclamide '5 mg/kg'). While GIV (SBEka, 60 mg/kg), GV (SBEKa, 120mg/kg) were respectively administered. After eighteen (18) days of oral administration of the extracts, the animals were sacrificed and the serum was collected for analysis of lipid profile (Total Cholesterol 'TC', Low Density Lipoprotein-Cholesterol 'LDL-C', High Density Lipoprotein-Cholesterol 'HDL-C', Very Low Density Lipoprotein 'VLDL' and Triglycerides 'TG'). The extract treated group showed significant decreased ($P<0.05$) serum level of TC, TAG, LDL cholesterol, VLDL, and AI while HDL significantly increase ($P<0.05$) compared to diabetic untreated control group. There is a decrease in blood glucose (BG) levels and lipid profile was evaluated for eighteen days of oral administration of the extracts. These results have justified the indigenous use of the plant against diabetes mellitus.

KEYWORDS: Diabetes mellitus; Alloxan; *Kigelia Africana;*lipoprotein; phytochemical compound.

INTRODUCTION

Diabetes mellitus (DM), or just diabetes, is a serious endocrine disorder either as a result of a lack of insulin or lack of insulin action. While the former is termed type I DM, the latter is referred to as type II DM (Kumar *et al*; 2011, and Aminu *et al;* 2017). Diabetes mellitus has been considered as one of the major health concerns all around the world today (Kruger *et al;* 2012 and Said *et al;* 2019) and represents serious health chaos of global concern as it has already reached epidemic globally (Chen *et al*; 2015 and Aminu *et al*; 2017). It was reported that, about nine million people across developing and developed countries had DM in 2014 (Aminu *et al;* 2017). Approximately 7.1 million Africans by the year 2000 were reported to be suffering from DM with the figure expected to rise further to 18.6 million by 2030 (Wild, et al;2004). Nigeria is the most populous nation in Africa and the 7th most populous nation on earth. Current approximate population is 170 million and counting, with 76 million adults and 3.1 million people with DM (Health report, 2006; Osibogun, 2012 and Said *et al;* 2019). DM is so fatal that it was responsible for more than one and a half million deaths in 2012 (Aminu *et al;* 2017). Although the disease is prevalent amongst both developed and developing countries, its detrimental effects are skewed being more pronounced in the developing countries as compared to their developed, richer counterparts (Njogu *et al;* 2016). Diabetes often presents with a number of life-threatening complications and co-morbid conditions amongst which are hyperglycemia and hyperlipidemia (Chen *et al;* 2015 and Zhang *et al* 2009). The latter has been tipped among the leading causes of chronic cardiovascular diseases in patients with diabetes (Sarfraz *et al;* 2016). *Kigelia africana*, a member of the Bignoniaceae family, is appreciably ubiquitous on the African continent. It is abundantly found close to rivers and in wet savannah. *Kigelia africana* of the benth family (Rawiyya in Hausa) is abundant in the tropics and widely used in Nigeria as

herbal remedies for various ailments such as diarrhoea, malaria, rheumatism, retained placenta and dizziness (Gill, 1992). As far as we know, there is no publication on hypoglycemic and hyperlipidemic effect stem bark extracts of *Kigelia africana*.

MATERIALS AND METHODS

Chemicals
All the chemicals used were of analytical grade.

Collection and Identification of Plant.
The stem bark of the plant was collected from villages around Dutsinma Local government, Katsina state, Nigeria. Botanical identification was done at Botany unit and voucher specimen was deposited in the herbarium of the same institution for reference.

Preparation of the Extract
The dried stem bark was pounded using mortal and pistil, and then sieved to powder using a sieve. 200g of the powdered sample was dissolved in 1000ml of methanol and allowed to stay for 48 hours with periodic stirring. The sample was filtered using whatman number 1 filter paper, the filtrate was then placed in the ovum at 80^0 C, and complete drying took 8 hours. The extraction was repeated using 200g of the powdered part.

Experimental Protocol
A total of twenty five (25) rats of either sex weighed of 60 g to 100 g were used, and grouped into five (5) of six (5) rats each as follows:
Group I: Control rats administered only distilled water.
Group II: Diabetic control rats administered only distilled water.
Group III: Diabetic control rats administered orally Glibenclamide (5 mg/kg).
Group IV: Diabetic rats administered orally with SBEKa (60 mg/kg).
Group V: Diabetic rats administered orally with SBEKa (120 mg/kg).

At the end of the first week, two animals from each group were selected randomly and sacrificed the remaining three animals continue to receive the treatment for another week and were sacrificed at the end of the second week.

Induction of diabetes by Alloxan
Diabetes was induced in rats by a single Intraperitoneal (I.P.) injection of a freshly prepared solution of Alloxan (100 mg/kg) after 18 hours of fasting. The blood glucose level was monitored after alloxanization and blood samples collected by tail tipping method using a Glucometer. Seventy two hours later, the rats were observed to be diabetic.

Phytochemical Screening (Qualitative)
Saponins
- Frothing test: A $2cm^3$ of each extract was pipetted into five test tubes and each of the test tubes was shaken vigorously for 2minutes. Fronting indicated the presence of saponins.
- Emulsion test: Five drops of olive oil were added to cm^3 of each extract in four test tubes and the mixtures were vigorously shaken. A stable emulsion formed in the extract tested, indicated the presence of saponins.

Flavonoids
A $1cm^3$ of 10% NaOH was added to $3cm^3$ of each extract in five test tubes. The presence of yellow coloration indicated the presence of flavonoids.

Tannins
1. A $1cm^3$ of freshly prepared 10% KOH was added to $1cm^3$ of each extract in 5 test tubes. Appearance of a dirty white precipitate indicates the presence of tannins.
2. Two drops of 5% $FeCl_3$ were added to $1cm^3$ of each extract in five test tubes. A greenish precipitate observed indicated the presence of tannins.

Alkaloids
A $1cm^3$ of 1% HCL was added to $3cm^3$ of each extract in five test tubes. The mixture was heated for 20 minutes. It was cooled and filtered. The filtrate was used for the test using Wagner's reagent. Drops of Wagner's reagent were added to $1cm^3$ of each extract. A reddish-brown precipitate indicates the presence of alkaloid in the extract.

Cardiac Glycosides
A 1ml of the extract was pipetted in 5 different test tubes. Then, 2ml of 3.5% ferric chloride solution was added and allowed to stand for 1minute. One milliliter of concentrated H_2SO_4 was then carefully poured down the wall of the tube so as to form a cover layer. A reddish brown ring at the interface with the upper layer becoming green to blue indicated the presence of cardiac glycosides containing 2-deoxy sugar.

Volatile Oils
A small quantity of each of the extracts was shaken with dilute Hcl. The absence of a white precipitate which was to be performed indicated the absence of volatile oils.

Steroids
This will be carried out according to the method of (Habon, 1973). Then 1ml of the extract was dissolved in 2ml of chloroform, sulphuric acid was carefully added to form lower layer. A reddish brown colour at the interface indicated the presence of steroidal ring (1.e aglycone portion of the cardiac glycoside).

Anthraquinones
Five gramme (5g) of the plant extract was shaken with 10ml benzene, filtered and 5ml of 10% ammonia solution was added to the filtrate. The mixtures were shaken and the presence of a pink, red, or violent colour

in ammonical (lower) phase indicates the presence of free anthraquinones.

Estimation of glucose levels

Serum glucose was estimated by glucose oxidase method using Randox kit (Barham., et al., 1972.).

Estimation of serum lipid profile levels

Serum Total Cholesterol (TC) (Allain., et al., 1974), High-Density Lipoprotein Cholesterol (HDL-C) (Burstein, et al., 1970) and Triglycerides (TAG) (Trinder, 1969). were quantified by an enzymatic method using Randox kit. LDL-C and VLDL-C were calculated using friedewald formula (Friedewald, et al., 1972).

- LDL-C (mmol/l) =TC- (HDL-C)-TG/2.2
- VLDL-C (mmol/l) =TG/2.2

The atherogenic index was calculated using the formula as described by (Shinde, et al., 2013).

- Atherogenic index (AI) =Total cholesterol-HDL Cholesterol/HDL Cholesterol

Statistical Analysis

The Statistical Package for Social Sciences (SPSS) Computer software version 16 was used for data analysis. The results were expressed as mean ± standard deviation (S.D) with the results analyzed by using one-way analysis of variance (ANOVA). Post-Hoc Dunnett's-test at 95% level of significance was used to assess the significant difference between the control and treated groups. P<0.05 was considered to be statistically significant.

RESULTS

Table 1: Phytochemical Constituents of the Stem Bark extract of *Kigelia Africana.*

	METHANOL EXTRACT
FLAVANOIDS	+++
ALKALOIDS: Wagners	+++
TANNINS	+
CARDIAC GLYCOSIDES	+
ANTHRAQUINONE	+++
SAPONINS	+++
STEROIDS	+++
VOLATILE OILS	**-Ve**

Qualitative

Key:
+ = Moderate
+++ = High
-Ve = Not present

Serum glucose level

Table 2 shows the effect of *Kigelia Africana* extracts on fasting blood glucose (FBG) level which were measured on 5th, 7th, 9th, 11th, 14th, 16th and 18thday of post induction and compared with normal and diabetic control groups. The values in the table below of Alloxan-induced rats showed a significant increase (P<0.05) in the fasting blood glucose (FBG) level compared to normal rats. Oral administration of methanolic stem bark extract of *Kigelia africana* (SBEKa) at the dose of 60 mg/dl and 120 mg/dl body weight showed a normal FBG level on a 14th day when compared with the normal control. The group orally administered glibenclamide 5 mg/kg body weight showed a normal glucose level.

Table 2: Effect of administration of methanolic stem bark extract of *K.africana* on glucose levels in alloxan induced diabetic rats for 18 days.

Group treatment	Before induction	72 hours after induction	7th day induction & extract administered	9th day induction & extract administered	11th day induction & extract administered	14th day induction & extract administered	16th day induction & extract administered	18th day induction & extract administered
GI NC	51.00±2.92^{a}	91.80 ± 4.24^{a}	84.80 ± 4.68^{a}	90.60 ± 5.26^{a}	91.20 ± 3.32^{a}	92.20 ± 2.62^{a}	89.60 ± 7.28^{a}	96.00 ± 4.30^{a}
GII DC	59.80 ± 5.00^{a}	245.80±57.59^{b}	271.40 ± 54.28^{b}	331.6 ± 59.25^{b}	339.08 ± 52.08^{b}	349.08 ± 52.08^{b}	352.2 ± 55.72^{b}	376.4 ± 56.84^{b}
GIII GLB 5mg/kgb.w	50.60 ± 2.25^{a}	300.00 ± 9.74^{c}	231.00 ± 10.78^{b}	238.33 ± 15.18^{c}	144.2 ± 15.18^{c}	134.2 ± 15.18^{c}	127.40 ± 9.16^{c}	105.80 ± 3.07^{c}
GIVSBEKa 60mg/kg b.w	52.00 ± 4.77^{a}	313.60±68.97^{c}	263.20 ± 46.61^{b}	206.45 ± 7.76^{c}	190.2 ± 7.76^{c}	180.2 ± 6.66^{c}	188.20 ± 39.87^{c}	118.20 ± 10.00^{c}
GV SBEKa 120mg/kg b.w	56.00 ± 5.32^{a}	332.40±52.22^{c}	246.00 ± 28.32^{b}	190.08 ± 5.99	138.6 ± 5.99^{c}	128.6 ± 5.99^{c}	121.80 ± 7.17^{c}	107.2 ± 5.29^{c}

Values are Mean ± SD of 5 determinations. Values with different alphabetical superscript along a column are significantly different at P<0.05, n=5, NC= Normal Control, DC= Diabetic control, GLB= Glibenclamide, SBEKa= 2: SBEKa= stem bark extract of *Kigelia africana* B.W: Body weight **Note:** a, b and c show statistical differences along the column.

Serum lipid profile for first week

Table 3 shows significant increased (P<0.05) serum level of total cholesterol, HDL cholesterol and LDL cholesterol, while triglycerides VLDL and Artherogenic index (AI) shows a significant decrease (P<0.05) compared to normal control. The standard drug-treated group shows significant decreased (P<0.05) in HDL Cholesterol, LDL, and significant increased (P<0.05) in triglyceride, VLDL and AI with normal total cholesterol when compared with Diabetic control. The extracts treated group shows significant increased (P<0.05) in all parameters in (Group IV) and total cholesterol, AI with normal HDL-cholesterol and significant decreased in triglyceride, LDL cholesterol and VLDL (Group V) when compared with the (Group 1). Total cholesterol, VLDL and AI show a significant increased (P<0.05) and significant decreased in HDL cholesterol, triglyceride, LDL cholesterol level when compared with the Group II.

Table 3: Effect of administration of methanolic stem bark extract of *K.africana* on lipid profile parameters in alloxan induced diabetic rats for 7 days.

Group Treatment	T.CHOL mMol/L	HDL-C mMol/L	TAG mMol/L	LDL-C mMol/L	VLDL-C mMol/L	Artherogenic Index (AI) mMol/L
GI NC	2.25 ± 0.05^{a}	0.68 ± 0.00^{a}	0.93 ± 0.04^{a}	1.15 ± 0.03^{a}	0.42 ± 0.02^{a}	2.31 ± 0.05
GII DC	2.40 ± 0.10^{a}	0.82 ± 0.05^{b}	0.78 ± 0.10^{b}	1.38 ± 0.25^{b}	0.35 ± 0.04^{b}	1.93 ± 0.13
GIII GLB 5mg/kg B.W	2.40 ± 0.30^{a}	0.76 ± 0.10^{c}	0.90 ± 0.14^{a}	1.24 ± 0.15^{c}	0.41 ± 0.06^{a}	2.16 ± 0.23
GIV SBEKa 60mg/kg	2.55 ± 0.45^{a}	0.75 ± 0.08^{c}	1.19 ± 0.52^{a}	1.27 ± 0.14^{c}	0.54 ± 0.24^{a}	2.40 ± 0.06
G V SBEKa 120mg/kg	$2.50 \pm O.50^{a}$	0.68 ± 0.01^{a}	0.53 ± 0.01^{b}	1.09 ± 0.01^{a}	0.24 ± 0.01^{b}	2.68 ± 0.21

Values are Mean ± SD of 2 determinations. Values with different alphabetical superscript along a column are significantly different at P < 0.05, n=5, SBEKa = 2, GLB= Glibenclamide. NC= Normal control, DC= Diabetic control, AI = Artherogenic index

Serum lipid profile for second week

Table 4 shows significant increased (P<0.05) serum level of total cholesterol, triglyceride, LDL cholesterol, VLDL, AI while HDL shows a significant decrease (P<0.05) compared to normal control. The standard drug-treated group shows significant decreased (P<0.05) in all the parameters when compared with Diabetic control group. The extracts treated group shows significant decreased (P<0.05) in all parameters compared to diabetic control group and significant increase in Total cholesterol, triglyceride, LDL, VLDL, AI and significant decrease in HDL cholesterol and shows normal Triglyceride (Group V) compared to normal control group.

Table 4: Effect of administration of methanolic stem bark extract of *K.africana* on lipid profile parameters in alloxan induced diabetic rats for 14 days.

Group Treatment	T.CHOL-mMol/L	HDL-C mMol/L	TAG mMol/L	LDL-C mMol/L	VLDL-C mMol/L	Artherogenic Index (AI) mMol/L
G I NC	2.05 ± 0.17^{a}	0.95 ± 0.09^{a}	0.76 ± 0.02^{a}	0.79 ± 0.01^{a}	0.34 ± 0.01^{a}	1.16 ± 0.15
G II DC	3.67 ± 0.09^{b}	0.66 ± 0.01^{b}	1.28 ± 0.30^{b}	2.49 ± 0.02^{b}	0.57 ± 0.14^{b}	4.56 ± 0.53
G III GLB 5mg/kg B.W	2.81 ± 0.15^{a}	0.62 ± 0.06^{b}	0.66 ± 0.61^{c}	1.86 ± 0.26^{c}	0.52 ± 0.31^{b}	3.53 ± 0.40
G IV SBEKa 60mg/kg	2.68 ± 0.10^{a}	0.67 ± 0.15^{b}	0.89 ± 0.07^{a}	1.54 ± 0.08^{c}	0.41 ± 0.03^{ab}	3.25 ± 0.41
G V SBEKa 120mg/kg	2.5 ± 0.15^{a}	0.79 ± 0.10^{b}	0.76 ± 0.10^{a}	1.60 ± 0.12^{c}	0.48 ± 0.05^{ab}	1.87 ± 0.31

Values are Mean ± SD of 3 determinations. Values with different alphabetical superscript along a column are significantly different at P<0.05, n=5, SBEKa = 2, GLB= Glibenclamide. NC= Normal control, DC= Diabetic control

DISCUSSION

The study showed that after 2 weeks treatment with methanolic SBEKa on diabetic and non-diabetic rats showed significant reduction effect (P<0.05) on their blood glucose level (Table 2). GIV and GV show that all doses of extract significantly (P<0.05) lowered blood glucose levels on the 18th day, but the Group V extract is more effective in such a way it returns the blood glucose level to normal. The Group V extract shows a similar

effect with the standard drug. This indicates a positive effect of methanolic SBEKa on the 18th day of oral administration in reducing the blood sugar levels. There is a marked increase in sugar level (hyperglycemia) in diabetic rats. The result agrees with already existing literature that alloxan induces diabetes mellitus by selectively destroying the beta cells of the pancreas which are involved in the synthesis of, storage and release of insulin, as well as the peptidehormone regulating carbohydrate, protein and lipid metabolism leading to marked increase in blood glucose concentration observed in rats after administration and confirms the development of diabetes mellitus (Akindele *et al*, 2012 and Said et al; 2019). The treatment goal for diabetes mellitus is to prevent or reduce the risk and severity of complications associated with it. This goal is best achieved by maintaining normal or near normal blood glucose and lipid profile levels. There is a marked increase in sugar level (hyperglycemia) in diabetic rats. The extract may have achieved hypoglycemic and hypolipidemic property through increased insulin secretion, increased peripheral utilization of glucose, inhibition of endogenous glucose production or by inhibition of intestinal glucose absorption as reported in existing literature (Bakirel *et al*, 2007).

After first week of treatment the diabetic control rats had elevated mean total cholesterol, High density lipoprotein (HDL), low density lipoprotein cholesterol (LDL_C), with decreased Triglyceride (TAG), very low density lipoprotein cholesterol (VLDL-C) and Artherogenic index (AI) (Table 3). The extract of *Kigelia africana* had shown a hypolipidemic effect in diabetic rats. The group IV and V extract significantly reduced ($P<0.05$) HDL and LDL and at higher concentration (120mg/kg) TAG and VLDL levels decreased compared to the diabetic control group. Significant increased ($P<0.05$) in the serum TC, TAG, VLDL and AI for GIV and GV were observed in diabetic treated groups when compared with diabetic untreated group (GII). A significant increase ($P < 0.05$) in TC, TG, LDL_C, VLDL and AI with significant decreased in HDL-C (GIV and GV) and TAG, VLDL, LDL (GV) were observed when compared to the GIII treated with Glibenclamide (5 mg/kg). Table 4 the extract treated group showed significant decreased ($P<0.05$) serum level of TC, TAG, LDL cholesterol, VLDL, and AI while HDL significantly increase ($P<0.05$) compared to diabetic untreated control group. The cholesterol, triglyceride, and LDL lowering effect coupled with HDL elevating effect of an extract may help in reducing complications associated with hyperlipidemia as a result of diabetes mellitus (lee *et al;* 2000, Chase, 2000 and Said *et al;* 2019).

Phytochemical screening of the stem bark of (*Kigelia africana*) extract was found to contain some secondary metabolite. From the result, flavonoids, alkaloids, tannins, cardiac glycoside, anthraquinones, saponins and steroids were found to be present in methanol extract. These photochemical have been reported to have pharmacological properties. They are used by phytochemist in the production of drugs. They are used as growth regulators and as insect repellants example alkaloid. They are also used in synthesis of steroid hormones; fire extinguisher e.t.c. The use of secondary plants constituents as drugs by large number of phytochemists is an indication that medicinal plants are important natural sources of potential new drugs.

CONCLUSION AND RECOMMENDATION

In conclusion, results obtained from the studies reveal the hypoglycemic and hypolipidemic properties of SBEKa. SBEKa is much effective at higher concentration (120mg/kg). The treated group had shown a similar effect compared with the standard antidiabetic drug (glibenclamide). SBEKa could be used in the treatment and management of diabetes mellitus and its related complications. Further work on the mechanism of action and the isolation of the active compounds of the plant are recommended.

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