



## Antidiabetic, Antioxidant and Hypolipidemic Potentials of *Sterculia Setigera* Methanol Stem Bark Extract in Alloxan-Induced Diabetic Rats

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### Abstract

**Background:** *Sterculia setigera* is one of the medicinal plants used traditionally to treat various diseases with the insertion of diabetes. Diabetes mellitus is a prolonged metabolic disorder recognized as a hyperglycemia. The present study aimed at investigating the antidiabetic activity of the methanol stem bark extract of *Sterculia setigera*.

**Methods:** LD<sub>50</sub> screening was evaluated using standard methods. The sub-chronic effect of *Sterculia setigera* methanol stem bark extract on body weight, antidiabetic, antioxidant, lipid profile and histopathology were evaluated in Alloxan-induced diabetic rats, respectively.

**Results:** Acute toxicity study of methanol stem bark extract of *Sterculia setigera* revealed no mortality in the animals at the limit dose of 5000 mg/kg during the 14 days observation period. In the in vivo study, alloxan was capable of inducing diabetic conditions as there was a significant increase ( $P<0.05$ ) in the fasting blood glucose (FBG) of the entire induced groups compared with normal control. Groups treated with crude extract of *Sterculia setigera* (100-400 mg/kg) and the standard drug (glibenclamide) showed a significant decrease ( $P<0.05$ ) in FBG compared with diabetics control. There were significant reductions ( $p<0.05$ ) in serum TC, TG, VLDL, LDL, CAT, SOD, GPx, Vit E, Vit A, and MDA against diabetic control. On the other hand, significant increments ( $P<0.05$ ) in body weight and HDL were observed in the treated groups compared to diabetic control diabetic. Histopathological examination showed improvement in the regeneration of pancreatic  $\beta$ -cells islets.

**Conclusion:** In conclusion, *Sterculia setigera* stem bark extract exhibit hypoglycaemic, hypolipidemic, and antioxidant effects justifying its ethnomedicinal use for the treatment of diabetes.

**Keywords:** Antidiabetic, Alloxan, *Sterculia setigera*, Hypolipidemic, Antioxidant, Glibenclamide..

## 1. Introduction

Diabetes mellitus (DM) is a chronic metabolic disorder associated with high blood glucose levels as a result of insulin deficiency, abnormal insulin response or in some cases both [1]. Diabetes mellitus complications are in rapid growing currently in every part of the world [2]. Diabetes is classified into type-1 (T1DM) characterized due insulin deficiency and type-2 (T2DM) refers to insulin inefficiency [3]. People (Patients) with diabetes are mostly affected by any one of the complications such as cardiovascular disease especially hypertension, atherosclerosis, cardiomyopathy and microvascular damage [4]. Moreover, hyperglycemia and several other abnormalities such as imbalance of lipid homeostasis and oxidative stress are involved in the generation of diabetes-related cardiovascular complications, which are the major causes of morbidity and mortality of patients with diabetes [5]. Presently, managing of diabetes and its complication without adverse effect is still a major challenge to the medical practitioners. The use of conventional drugs in the treatment of diabetes is regulated by their pharmacokinetic properties [6]. Thus, exploring new class of therapeutic compounds for the treatment of diseases is of benefit to overcome diabetes difficulties. Currently, a lot of efforts have been made to search for alternative drugs that are cheaper, easy to store and possess no or fewer side effects [7]. Herbal medicine (preparations) is used to treat diabetes traditionally, as an alternative therapy [8]. Selected plants extracts have been reported to exert their antidiabetic effects by stimulating insulin release from the pancreatic beta cells. These plants include the aqueous leaf extract of *Aegle marmelos*, the ethyl ether extract of *Allium sativum* [9], and the leaves

extract *Diodia sarmentosa* [10]. *Sterculia setigera* Del is a multipurpose savannah tree with a wide ecological spread in tropical Africa. It is found mostly in the wild nature. In Nigeria it has various common names: English (karaya gum), Hausa (Kukuki), Fulani (bo'boli), and Yoruba (Ose-aware), [11]. The stem bark of *Sterculia setigera* has been reported to be used by traditional medicine practitioners in northern Nigeria to manage several diseases [12].

*Sterculia setigera* is one of the plants used in traditional medicine. Therefore, the present study seeks to address the *in vivo* antidiabetic activity of *Sterculia setigera* in Alloxan-Induced Diabetic Rats.

## 2. Materials and Methods

### 2.1. Materials chemical/reagents and equipment/instrumentation

All chemicals and equipment used were of analytical grade.

#### 2.1. Plant collection and identification

The fresh stem bark of *Sterculia setigera* was collected in November, 2020 at local farm Lands Zuru Local Government Area, Kebbi State. A Taxonomist identified and authenticated it, at the Botany Unit department of Plant Science and Biotechnology, Kebbi State University of Science and Technology, Aliero. Voucher specimens (KSUSTA/PSB/H/VOUCHER NO: 83B) have been deposited in the Herbarium of the same institution for further reference.

#### 2.1.4. Anti-diabetic conventional drug

Glibenclamide were purchased in December, 2020 from Hamdala Pharmacy Birnin Kebbi, Kebbi State.

## 2.2. Methods

### 2.2.1. Preparation of plant material

The stem bark of the plant was shade dried at room temperature for seven days to remove moisture content. Dried stem bark of plant were powdered in a clean mortar and pestle. The powdered material was sieved and stored in a sterile, tight container until needed. Two hundred Fifty grams (500 g) of powdered plant material was weighed and subjected to cold maceration using 2.5L of methanol and was allowed to stand for 75 hours with occasional turning and shaking. The mixture was filtered afterward with a clean white Muslim cloth. The filtrate obtained was evaporated to dryness using a rotary evaporator at 45 °C [13].

### 2.3. Experimental animals

Healthy male and female Wister albino rats weighing between 120-200 g were used for this study. The rats were fed with standard feed and water ad libitum, throughout the study [14]. All the procedure required in the control and experiments were carried out according to standard methods approved by the Animal Ethics Committee of Kebbi State University of Science and Technology Aliero.

### 2.4. Acute toxicity test

13 animals of both sexes were used for the determination of the acute toxicity of the plant extract. This test was conducted in two-phase. First phases, nine animals of both sexes were randomly divided into three groups with three rats each 1<sup>st</sup>, 2<sup>nd</sup> and 3<sup>rd</sup> groups received 10, 100, and 1000 mg/kg of the extract where mortality was observed within 48 hrs and others sign of toxicity. In the second phase, four rats were used one per group 1200, 1600, 2900, and 5000 mg/kg each [15]. Lethal Dose (LD<sub>50</sub>) was calculated using Lork formula:

$$\text{Lethal Dose} = \sqrt{D_0 \times D_{100}} \text{ [16]}$$

Where D<sub>0</sub>=Highest dose that cause no mortality, D<sub>100</sub>=Lowest dose that produce mortality

### 2.5. Induction of diabetes mellitus using alloxan monohydrate

Diabetes mellitus was induced using overnight fasted experimental rats by a single intraperitoneal injection of 120 mg/kg body weight of rats. Alloxan monohydrate was dissolved in 0.9% normal saline that serves as a vehicle. In the first 12 hrs, after diabetes mellitus was induced the rats were provided with 5% glucose solution as drinking water in order to avoid hypoglycemic shocked [17]. Confirmation was done 3 days after intraperitoneal injection of alloxan monohydrate, with On-call plus glucometer using blood samples obtained via tail puncture of the rats. After 72 h for development of diabetes, blood glucose was measured and rats with fasting blood glucose >200 mg/dl were considered as diabetic and used in the present study [18].

#### 2.5.1. Grouping and treatment

In the present investigation, a total of 30 rats (25 diabetic surviving rats and 5 normal rats) were taken and divided into six groups of 5 rats each.

Group I: Normal rats received 0.5mL of Normal Saline

Group II: Diabetic control rats received 0.5mL of Normal Saline

Group III: Alloxan-induced diabetic rats + 100mg/kg BW of *S. setigera*

Group IV: Alloxan-induced diabetic rats + 200mg/kg BW of *S. setigera*

Group V: Alloxan-induced diabetic rats + 400mg/kg BW of *S. setigera*

Group VI: Alloxan-induced diabetic rats + 5 mg/kg BW standard drug (glibenclamide).

The body weight of the animals was evaluated on the 1<sup>st</sup>, 7<sup>th</sup>, 14<sup>th</sup> and 21<sup>th</sup> days of the experiment.

## 2.6. Evaluation of biochemical parameters

Fasting blood glucose levels of the animals were evaluated on days 1, 7, 14 and 21 of the experiment using fine test glucometer. Malondialdehyde (MDA) was assayed according to the method of [19]. Catalase (CAT) was assayed according to the method [20]. Glutathione peroxidase (GPx) was assayed according to the method [21]. (SOD) was assayed by the method [22]. Vitamin A was determined according to the standard method [23]. Vitamin E was determined according to the standard method [24]. Serum total cholesterol (TC), total triglycerides (TG) and high-density lipoprotein cholesterol (HDL-C) [25], low density lipoprotein cholesterol (LDL C) and very low-density lipoprotein cholesterol (VLDC) [26] were analysed.

## 2.7. Histological examination of pancreas

The experimental animals were killed using anesthetizing chemical (chloroform) and histological examination of the pancreas was done using standard method described by [27].

## 2.8. Statistical analysis

Data were expressed as mean  $\pm$  SEM. Statistical comparisons was performed

by one-way analysis of variance (ANOVA) using SPSS package version 20.0. The significant difference ( $P < 0.05$ ) between the treated and untreated control group was established by Duncan multiple of comparison test.

## 3. Results

### 3.1. Acute toxicity and lethality (LD<sub>50</sub>) test:

Oral acute toxicity study of *Sterculia setigera* methanol stem extract revealed that the LD<sub>50</sub> is  $\geq 5000$  mg/kg.

### 3.2. Effect of *sterculia setigera* treatment on body weight

Normal rats showed a progressive increase in body weight in the study period (week 0-3). Hence, it is in contrast to diabetic control rats that showed a progressive reduction in the body weight throughout the study period (Table 1). Diabetic rats treated with SSME and glibenclamide revealed no significant difference ( $p < 0.05$ ) compared with diabetic group in week 0. But Diabetic rats treated with SSME (100-400 mg/kg) and glibenclamide (5 mg/kg) showed a significant ( $P < 0.05$ ) increase in bodyweight compared to diabetic untreated rats throughout the weeks.

**Table 1.** Effect of *S. setigera* Methanol Stem Extract on Body weight

Treatment (Dose)	WEEK0	WEEK1	WEEK2	WEEK3
Normal Control	190.85 $\pm$ 13.00 <sup>a</sup>	218.80 $\pm$ 15.33 <sup>a</sup>	218.97 $\pm$ 16.38 <sup>a</sup>	220.90 $\pm$ 18.41 <sup>a</sup>
Diabetic Control	148.52 $\pm$ 1.05 <sup>b</sup>	134.94 $\pm$ 4.19 <sup>c</sup>	131.50 $\pm$ 4.84 <sup>c</sup>	126.30 $\pm$ 4.60 <sup>c</sup>
SSME (100 mg/mL)	133.12 $\pm$ 6.37 <sup>b</sup>	116.60 $\pm$ 10.52 <sup>b</sup>	135.80 $\pm$ 5.27 <sup>b</sup>	138.32 $\pm$ 7.48 <sup>b</sup>
SSME (200 mg/m)	121.00 $\pm$ 1.71 <sup>b</sup>	109.02 $\pm$ 8.70 <sup>c</sup>	123.40 $\pm$ 4.37 <sup>b</sup>	125.47 $\pm$ 4.00 <sup>c</sup>
SSME (400 mg/mL)	144.32 $\pm$ 5.78 <sup>b</sup>	158.95 $\pm$ 7.96 <sup>b</sup>	165.35 $\pm$ 5.01 <sup>b</sup>	172.65 $\pm$ 2.49 <sup>b</sup>
Glibenclamide (5 mg/mL)	114.82 $\pm$ 9.31 <sup>b</sup>	105.05 $\pm$ 6.23 <sup>ec</sup>	128.90 $\pm$ 11.75 <sup>d</sup>	130.15 $\pm$ 10.59 <sup>d</sup>

Values are presented as mean  $\pm$  SEM (n = 4) values having the same superscript are not significantly different at (P<0.05) analysed using One-Way ANOVA, followed by Duncan multiple comparison test with SPSS version 20.0. {Group 1(normal control), group 2 (diabetic control), group 3 (SSME 100 mg/kg b.w), group 4 (SSME200mg/kg b.w), group5 (SSME 400 mg/kg b.w) and group 6 (standard drug 5 mg/kg b.w), SSEM = *Sterculia setigera* methanol extract.

### 3.3. Antidiabetic effect of *s. setigera* methanol stem bark extract in alloxan-induced rats

Induction with Alloxan monohydrate revealed an elevation of fasting blood glucose (FBG) level which mimics diabetic state compared with the normal

control (Table 2). In course of treatment with SSME (100-400 mg/kg) and glibenclamide (5 mg/kg) revealed a significant (P<0.05) decreased in fasting blood glucose compared to diabetic rats (Table 2).

**Table 2.** Antidiabetic Effect of *Sterculia setigera* Methanol Stem Bark Extract

Treatment (Dose)	Day-1 (mg/dl)	Day-7 (mg/dl)	Day-14 (mg/dl)	Day-21 (mg/dl)
Normal control	93.60 $\pm$ 8.72 <sup>a</sup>	87.30 $\pm$ 5.95 <sup>a</sup>	97.55 $\pm$ 6.89 <sup>a</sup>	79.00 $\pm$ 5.29 <sup>a</sup>
Diabetic control	378.00 $\pm$ 36.76 <sup>b</sup>	431.53 $\pm$ 27.63 <sup>c</sup>	446.68 $\pm$ 23.26 <sup>d</sup>	530.18 $\pm$ 22.80 <sup>c</sup>
SSME (100 mg/kg)	436.08 $\pm$ 63.44 <sup>b</sup>	400.95 $\pm$ 44.73 <sup>bc</sup>	357.00 $\pm$ 24.89 <sup>bc</sup>	307.78 $\pm$ 41.44 <sup>b</sup>
SSME (200 mg/kg)	427.50 $\pm$ 57.16 <sup>b</sup>	267.93 $\pm$ 30.12 <sup>b</sup>	290.78 $\pm$ 78.99 <sup>bc</sup>	216.28 $\pm$ 39.16 <sup>b</sup>
SSME (400 mg/kg)	369.90 $\pm$ 82.17 <sup>b</sup>	273.60 $\pm$ 48.69 <sup>b</sup>	152.90 $\pm$ 13.77 <sup>ab</sup>	211.88 $\pm$ 42.84 <sup>b</sup>
Glibenclamide (5 mg/kg)	407.73 $\pm$ 54.23 <sup>b</sup>	336.58 $\pm$ 76.47 <sup>bc</sup>	205.58 $\pm$ 75.12 <sup>ab</sup>	228.75 $\pm$ 59.35 <sup>b</sup>

Values are presented as mean $\pm$ SEM (n=4) values having the same superscript are not significantly different at (P<0.05) analysed using One-Way ANOVA, followed by Duncan multiple comparison test with SPSS version 20.0. {(Group I=normal control, group II diabetic control), (group III treated with 100 mg/kg BW), (group IV treated with 200 mg/kg bw), (group v treated with 400 mg/kg BW) and (group vi treated with 5 mg/kg BW of standard drug), SSME= *Sterculia setigera* methanol extract.

### 3.4. Antioxidant effects of ssme in alloxan-induced diabetics rats

There was a significant (P<0.05) reduction in catalase (CAT), superoxide dismutase (SOD), glutathione peroxidase (GPx), vitamin A (Vit A) and vitamin E (Vit E) in all alloxan-induced diabetic rats (Table 3). However, treatment with SSME (100-400 mg/kg) and glibenclamide (5 mg/kg) did not ameliorate these effects compared with diabetic control. On the other hand, MDA levels were elevated by Alloxan induction was significantly (P<0.05) decreased upon treatment with SSME (100-400mg/kg) and

glibenclamide (5 mg/kg) compared with diabetic control.

### 3.5. Effects of SSME on lipid profile in alloxan-induced diabetic rat

After successful induction of diabetes using Alloxan monohydrate there was a significant (p<0.05) increase in serum TC, TG, LDL AND VLDL and a decrease in HDL compared with normal control (Table 4). However, treatment with SSME (100-400 mg) and glibenclamide (5 mg/kg) to Alloxan-induced diabetic rats for 21 days significantly (p<0.05) reduced serum TC, TG, LDL and VLDL

levels with an increase in serum HDL level in a dose-related manner compared with diabetic rats (Table 4).

**Table 3.** Antioxidant Effects of *S.setigera* Methanol Stem Bark in Alloxan-induced Rats.

Treatment (Dose)	VIT. A (mg/dl)	VIT. E (mg/dl)	SOD ( $\mu\text{mol/g}$ )	CAT ( $\mu\text{mol/g}$ )	GPx ( $\mu\text{mol/g}$ )	MDA (nmol/mL)
Normal control	6.50 $\pm$ 0.37 <sup>c</sup>	3.11 $\pm$ 0.25 <sup>c</sup>	10.41 $\pm$ 0.77 <sup>d</sup>	50.39 $\pm$ 1.02 <sup>c</sup>	25.09 $\pm$ 1.10 <sup>c</sup>	4.53 $\pm$ 0.43 <sup>a</sup>
Diabetic control	4.59 $\pm$ 0.84 <sup>ab</sup>	2.81 $\pm$ 0.67 <sup>bc</sup>	7.37 $\pm$ 1.40 <sup>c</sup>	39.05 $\pm$ 8.19 <sup>bc</sup>	18.11 $\pm$ 4.2 <sup>a</sup>	9.12 $\pm$ 0.53 <sup>c</sup>
SSME (100 mg/kg)	3.42 $\pm$ 0.57 <sup>ab</sup>	0.947 $\pm$ 0.29 <sup>a</sup>	4.90 $\pm$ 0.25 <sup>a</sup>	23.41 $\pm$ 1.32 <sup>a</sup>	12.67 $\pm$ 1.00 <sup>b</sup>	7.04 $\pm$ 0.60 <sup>b</sup>
SSME (200 mg/kg)	5.02 $\pm$ 0.35 <sup>bc</sup>	2.89 $\pm$ 0.26 <sup>bc</sup>	3.17 $\pm$ 0.28 <sup>a</sup>	36.04 $\pm$ 0.77 <sup>b</sup>	22.41 $\pm$ 0.77 <sup>d</sup>	5.32 $\pm$ 0.47 <sup>b</sup>
SSME (400 mg/kg)	4.35 $\pm$ 0.55 <sup>ab</sup>	1.87 $\pm$ 0.200 <sup>ab</sup>	4.90 $\pm$ 0.29 <sup>a</sup>	30.81 $\pm$ 4.28 <sup>ab</sup>	18.27 $\pm$ 2.36 <sup>b</sup>	6.18 $\pm$ 0.47 <sup>b</sup>
Glibenclamide (5 mg/kg)	3.03 $\pm$ 0.35 <sup>a</sup>	1.63 $\pm$ 0.13 <sup>a</sup>	5.47 $\pm$ 14 <sup>bc</sup>	30.08 $\pm$ 1.50 <sup>ab</sup>	14.00 $\pm$ .83 <sup>b</sup>	5.52 $\pm$ 0.45 <sup>b</sup>
Treatment (Dose)	VIT. A (mg/dl)	VIT. E (mg/dl)	SOD ( $\mu\text{mol/g}$ )	CAT ( $\mu\text{mol/g}$ )	GPx ( $\mu\text{mol/g}$ )	MDA (nmol/mL)

Values are presented as mean $\pm$ SEM (n=4) value having one of the same superscripts are not significantly different at ( $P<0.05$ ) analysed using One-Way ANOVA, followed by Duncan's multiple comparison test with SPSS version 20.0. (VIT.A=Vitamin A, VIT E=Vitamin E, SOD=Superoxidase, CAT=Catalase, GPx=Glutathione Peroxidase), SSME=*Sterculia setigera* methanol extract

**Table 4.** Effect of *S. setigera* Methanol Stem Bark Extract on Serum Lipid Profile

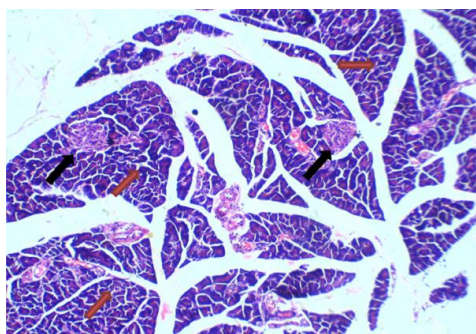
Treatments (Dose)	TC(mg/dl)	TG(mg/dl)	LDL(mg/dl)	VLDL(mg/dl)	HDL(mg/dl)
Normal Control	93.16 $\pm$ 5.64 <sup>a</sup>	82.72 $\pm$ 2.83 <sup>a</sup>	63.61 $\pm$ 4.44 <sup>a</sup>	16.20 $\pm$ 0.37 <sup>a</sup>	35.18 $\pm$ 0.42 <sup>b</sup>
Diabetic Control	177.12 $\pm$ 4.63 <sup>d</sup>	198.28 $\pm$ 5.95 <sup>e</sup>	151.20 $\pm$ 8.61 <sup>d</sup>	53.91 $\pm$ 2.57 <sup>e</sup>	26.06 $\pm$ 0.74 <sup>a</sup>
SSME (100 mg/kg)	137.15 $\pm$ 1.31 <sup>c</sup>	149.93 $\pm$ 3.40 <sup>d</sup>	132.8x9 $\pm$ 1.05 <sup>c</sup>	36.447 $\pm$ 4.96 <sup>d</sup>	28.67 $\pm$ 0.35 <sup>a</sup>
SSME (200 mg/kg)	127.91 $\pm$ 3.20 <sup>c</sup>	112.19 $\pm$ 3.67 <sup>c</sup>	79.74 $\pm$ 3.05 <sup>b</sup>	25.83 $\pm$ 0.79 <sup>c</sup>	26.84 $\pm$ 1.12 <sup>a</sup>
SSME (400 mg/kg)	107.52 $\pm$ 6.38 <sup>b</sup>	103.12 $\pm$ 3.10 <sup>bc</sup>	61.08 $\pm$ 5.18 <sup>a</sup>	22.47 $\pm$ 1.23 <sup>bc</sup>	35.49 $\pm$ 0.45 <sup>b</sup>

Values are presented as mean  $\pm$  SEM (n= 4) value having the same superscript are not significantly different At ( $P<0.05$ ) analyzed using OneWay ANOVA, followed by multiple comparison tests with SPSS version 20.0. The comparison was made between lipids level in serum samples of Alloxan-induced diabetic rats and SS and glibenclamide treated animals. Where TC=Total cholesterol, TG=Triglycerides, LDL=Low density lipoprotein VLDL=very-low-density lipoproteins, HDL=Highdensity lipoproteins. SSME=*Sterculia setigera* methanol extract.

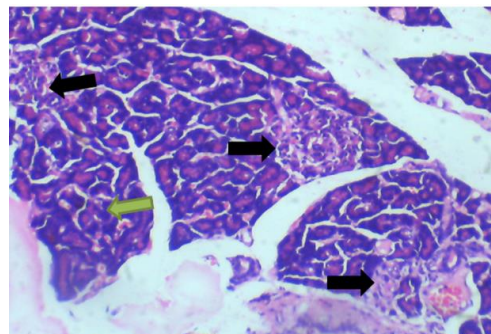
### 3.6. Effect of *s. setigera* on histopathology of pancreas in alloxan-induced rats

Histopathological studies of the normal control did not show any microscopic lesion around the islet tissues (plate 4.1). The diabetic non-treated group and diabetic rats treated

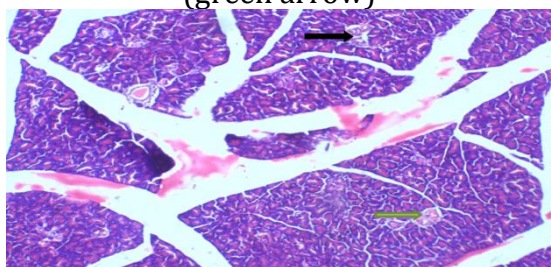
with extract (100 mg/kg) showed atrophy and fibrosis of islets tissue (plate 4.2 and 4.3). In SSME (200 and 400 mg/kg) and glibenclamide (5 mg/kg) treated rats showed improvement in islets of Langerhans regeneration (plate 4.4, 4.5 and 4.6) compared with diabetic rats (plate 4.2).



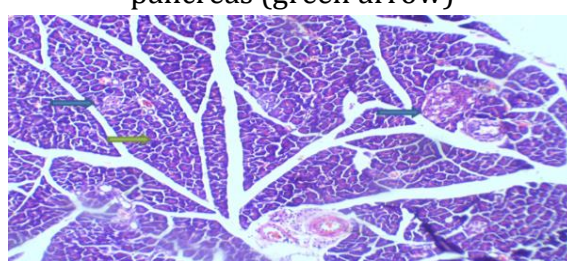
**Plate 1:** Photomicrograph of rat pancreas obtained from normal control (H and E X 200 magnification) showing the endocrine cells as pale stained (islets of Langerhans black arrow) and the dark stains cells of the surrounding as the exocrine pancreas (green arrow)



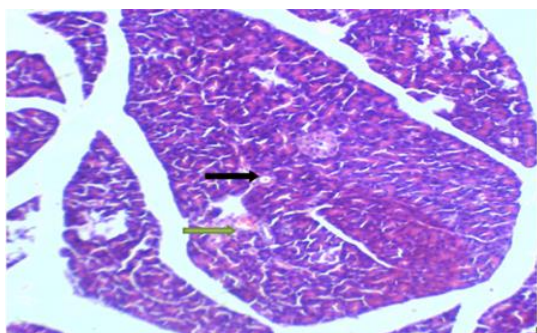
**Plate 2:** Photomicrograph of rat pancreas obtained From diabetic control (H and E X 200 magnification) Showing the endocrine cells as pale stained (islets of Langerhans arrow with fibrosis and the dark stains cells of the surrounding as the exocrine pancreas (green arrow)



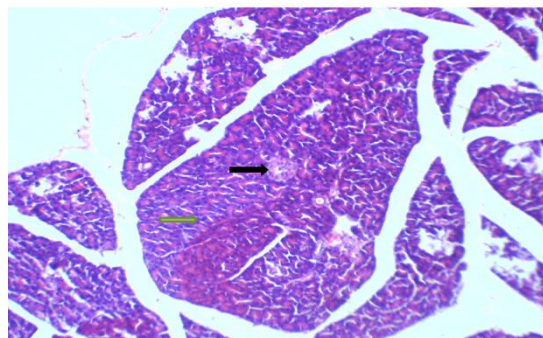
**Plate 3:** Photomicrograph of rat pancreas obtained from group-administered with 100 mg/kg of methanol stem bark extract of *S.setigera*. (H and E stain x 200 magnification) showing the endocrine cells as pale stained (islets of Langerhans black arrow with atrophy and fibrosis) and the dark stains cells of the surrounding as the exocrine pancreas (green arrow)



**Plate 4:** Photomicrograph of rat pancreas obtained from group-administered with 200 mg/kg of methanol stem bark extract of *S.setigera*. (H and E stain, x 200 magnification) showing the few endocrine cells as pale stained ( islets of Langerhans blue arrow with regeneration) and the dark stains cells of the surrounding as the exocrine pancreas (green arrow)



**Plate 5:** Photomicrograph of rat pancreas obtained from group administered with 400 mg/kg of methanol stem bark extract of *S.setigera*. (H and E stain x 200 magnification) showing islets of Langerhans black arrow with regeneration



**Plate 6:** Photomicrograph of rat pancreas obtained from group administered with 5 mg/kg of the standard drug (glibenclamide). (H and E stain, x 200 magnification) showing islets of Langerhans black arrow with regeneration

#### 4. Discussion

The present study was designed to find out the in vivo antidiabetic activity of methanol stem bark extract of *Sterculia setigera*. Presently, there is pronounced attention in plants source medicines and well-designed foods that modulate physiological activity in the prevention and controlling of DM [28]. DM is characterized by hyperglycemia and it is accompanied by loss of body weight [29-30].

Toxicological study is carried out to check the safety of drugs and plant products for human use. Toxicity of substances affects the health of organism, to ascertain the safety of plants base substances there is need to subject the plant product for toxicity analysis [31]. LD50 is the first step and important tool used in toxicology studies to determine how toxic substances are on different types of organisms and provides measures to compare and rank the toxicity of substances. According to a scientific report, 1 mg/kg is considered highly toxic, 10 mg/kg is considered toxic, 100 mg/kg is moderately toxic, 1000 mg/kg is slightly toxic, and 5000 mg/kg is considered not toxic [15]. Any plant with LD50 $\geq$ 5000 mg/kg implies that the plant extract is relatively safe for acute use. However, less activity in the movement and quietness observed in the animals treated with plant extract may be due to the presence of central nervous system depressant constituents in the plant extract [32-33]. LD50 result of the present study is in line with previous report that the mentioned substances with an LD50 value greater than 5g/kg are considered to cause no toxicity on acute administration [34-35]. Therefore, *Sterculia setigera* methanol stem bark extract is considered to be safe for acute use due to their higher LD50 value.

Diabetic conditions or insulin deficiency prevents the body cells from

the utilization of glucose and reflects the increase in glycogenolysis, lipolysis, and gluconeogenesis for the energy generation [36]. Thus, these biochemical events result in muscle wasting and loss of tissue protein that eventually give rise to the reduction of overall body weight [37]. Induction of diabetic condition with Alloxan or streptozotocin has been stated to cause body weight loss or reduction in mice and albino rats [38-39]. After treatment of diabetic rats with *Sterculia setigera* methanol stem bark extract, there is an improvement of their body weight. This research work is in corroboration with previous work reported by other researchers [40-41].

Alloxan monohydrate is a chemical substance that can come as a result of mechanism of action to attack  $\beta$ -cells of islets of Langerhans in the pancreas organ. This can bring about a decrease or lacking of endogenous insulin in the system and consequently affects the utilization of glucose by the tissues [42-43]. Increase in fasting blood glucose level is the most common feature of diabetes mellitus [44]. Decrease in blood glucose levels in diabetic rats may be due to the presence of hypoglycemic agents present in plant extracts that act either by stimulating the release of insulin, increase sensitivity of cells receptor or by inhibiting certain enzymes that catalyses carbohydrate to break down [45]. Glibenclamide stimulates the exocytosis of insulin from  $\beta$ cells of pancreas [45]. The present study revealed that *Sterculia setigera* methanol stem extract showed reduction in fasting blood glucose level, which may be to its ability to stimulate the secretion of insulin from  $\beta$ -cells of the pancreas or by increasing the peripheral glucose uptake. Similar effects were observed in previous research on root extract of *Cassia occidentalis* Linn [46].

Oxidative stress is an important mechanism for the induction and progression of diabetes and diabetic



complications, which results from an imbalance between pro-oxidants and antioxidants [47]. High amounts of free radicals generated due to hyperglycaemia cause glucose autoxidation and protein glycosylation, which bring about diabetes mellitus pathogenesis [48-49]. SOD, CAT, GPx, Vit A, Vit E, and MDA are antioxidants that protect the tissues against free radicals. Dismutating superoxide into molecular oxygen and hydrogen peroxide responsible for oxidative stress are detoxified via enzymatic and non-enzymatic activities [50-53]. Measurement of MDA, as final product of the lipid peroxidation, will reflect the degree of oxidative stress [54]. Indeed, reduction of MDA reflects the decrease in lipid peroxidation due to oxidative stress. But treatment of diabetic rats with plant extract revealed a decrease in serum MDA level [54]. In the current study, treatment of diabetic rats with *Sterculia setigera* was capable of reducing the concentration of MDA in the lipid profile alone but failed to improve the activity of enzymatic antioxidants and that of Vitamin A and Vitamin E.

Dyslipidaemia is another complication of diabetes mellitus that results in the elevation of plasma lipid profile including TC, LDLC, VLDL and triglycerides and decreases the concentration of HDLC [5]. Insulin deficit brings about activation of hormone sensitive lipase, which will cause the increase in lipolysis and secretion of VLDL from the liver [55]. Decrease in activity of lipoprotein lipase brings improper clearance of chylomicrons and VLDL [56-57]. The current study showed that the increment of lipid profile was observed in rats administered with alloxan alone and this finding corroborates with several other studies [58-59]. Decrease in serum lipid levels in diabetic rats after treatment with plant extract can be directly associated with an improvement in

insulin levels [60]. Similar effects were observed in diabetic rats treated with *Sterculia setigera* methanol stem bark extract.

Histopathological investigation of Alloxan induced diabetic rats have been reported to show destruction in islets of Langerhans [61]. Pancreas  $\beta$ -cells are sensitive to smash-up by free radicals generated by Alloxan and streptozotocin [62]. Degeneration of pancreas in diabetic rats is due to the necrotic action of alloxan monohydrate [61]. Previous studies have reported that different plant extracts have shown pancreas  $\beta$  cell regeneration due to their antioxidant activities [63-64]. This is in corroboration with the present study where islets of Langerhans regenerated in animals treated with *Sterculia setigera* methanol stem bark extract was observed.

## 5. Conclusion

The present study reports that *S. setigera* methanol stem bark extract (SSME) is non-toxic and possess hypoglycaemic, hypolipidemic and antioxidant potentials. This validates the folk use of this plant for the treatment of diabetes.

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## Ethics Approval and Consent to Participate

The authors declare that animals were used in this research therefore; the research was given the ethical approval code as follow (KSUSTA/FLS/FREC/20-03) from the university committee.

## Conflict of interest

The authors declare that there is no conflict of interest

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