EFFECT OF METHANOLIC FRUIT EXTRACT OF *BORASSUS AETHIOPUM* ON BODY MASS INDEX AND LIPID PROFILE PARAMETERS OF HIGH FAT DIET INDUCED OBESE WISTAR RATS

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ABSTRACT

Background: Obesity is a known global epidemic, mostly defined as an excess of body fat and described by the body mass index (BMI) which is calculated as the weight divided by square of height (w/h^2). Currently there is lack of scientific data on the effect of *Borassus aethiopum* fruit on obesity and lipid profile parameters.

Aim: The aim of this study was to evaluate the effect of *Borassus aethiopum* fruit on BMI and lipid profile parameters of high fat diet induced obese Wistar rats.

Methodology: A total of twenty-five (25) rats weighing approximately 90 to 105 g were randomly divided into five (5) groups of five (5) rats each, negative control group A were fed with a normal pellet diet (NPD), the remaining four (4) groups were fed with a high fat diet (HFD) for 12 weeks. The rats in group B, C and D were administered with different dose of the extract for 14 days. The LD_{50} of the extract was determined, Body mass index was calculated, Total Cholesterol, Triglycerides, HDL-Chol and LDL-Chol were assayed by enzymatic method.

Results: Results showed that, the extract has no toxic effect even at a dose of 5000 mg. there was a significant reduction in the BMI of rats administered with extract as compared with controls ($p< 0.05$). The extract has a reducing effect on T-Chol, TG and LDL-Chol levels ($p< 0.05$).

Conclusion: In conclusion, the extract is safe for consumption and help to reduce BMI and by extension help to improved lipid profile parameters.

Keywords: *Borassus aethiopum*, Body Mass Index, Lipid Profile, High Fat Diet, Obese, Wistar Rats

INTRODUCTION

Obesity is a known global epidemic, mostly define as an excess of body fat mass (Cercato and Fonseca, 2019), usually described by the body mass index (BMI). Obesity have been known to have very serious consequences with increased risk of morbidity and reduced life expectancy (Cercato and Fonseca, 2019). However, two (2) patterns of obesity have been distinguished for the purpose of risk factor assessment; namely, central (abdominal or visceral) obesity and peripheral obesity (Darvall *et al.,* 2007). Central obesity is said to be more dangerous and associated with high risk of morbidity and mortality.

Peripheral obesity on the other hand is generally due to subcutaneous fat while central obesity although partially subcutaneous yet involves more of the visceral organs (Lilian *et al.,* 2013). Generally, obesity have been associated with numerous disorders, such as type 2 diabetes mellitus, obstructive sleep apnea syndrome, gastrointestinal disorders, depression, malignancies, stroke and cardiovascular diseases including coronary artery disease, hypertension, and venous thromboembolism (VTE). The World Health Organization (WHO) reports show that the worldwide obesity nearly tripled since 1975, in 2016, 39% of adults were overweight and 13% were obese (Hotoleanu, 2020).

In Nigeria, its estimated that about 18% of adolescents are obese. Similarly, there is an increasing prevalence of obesity among women most especially of the childbearing age. This simply mean that, there would be an increase in the prevalence of chronic diseases such as cardiovascular diseases, thrombosis and other non-communicable diseases whose trend follows an increased prevalence of obesity (Eyam *et al.,* 2013), However, the prevalence of overweight and obesity in Nigeria and other developing countries is of epidemic proportions. Therefore, there is need to pay closer attention to combating these health disorders (El-Menyar *et al.,* 2018).

The plant *B. aethiopum* has been described as a palm tree with huge fan shaped leaves. In Nigeria, the Hausas call it *Giginya*, the Yorubas call it *Agbonolodu*, and the Igbos call it *Ubiri*. The plant is a dioecious plant and can reach up to 20 m high on average and 1 m in diameter (Muhammad *et al.,* 2019). It's an important food source providing edible fruits, and nuts. The sap obtained from the inflorescence is drunk raw or processed into wine, alcohol or vinegar and also dried into sugar cakes. In Ghana and other West African countries such as Ivory Coast, the ripe mature fruits are either boiled or used raw, the mesocarp is mashed, and the thick liquid obtained eaten with or without boiled maize as food. The flowers of *Borasus aethiopum* are also used to treat conditions such as impetigo and the roots for asthma, *Borasus aethiopum* has been shown to have antidiabetic role. It was also found to be nephron- and hepato-protective as well as boosting the immunity (Larbie *et al.,* 2016). The Borassus-fortified bread significantly reduced blood pressure and other metabolic risk factors among the CVD outpatients studied. Therefore, it has a curative role in the management of CVD (Apprey *et al.,* 2020). It has also been revealed to have activity against the gram-positive bacteria such as *Staphylococcus aureus* and *Bacillus subtilis*. The results obtained showed that *Borassus aethiopum* has anti-inflammatory and significant anti-oxidant properties (Sarkodie and Squire, 2015). However, this study was designed to principally investigate its role in obesity and anti-thrombotic activity on rats.

Obesity has become a threat to the health and economy of society worldwide and if not contained, will be responsible for a dramatic increase in cardiorespiratory diseases and certain cancers. It is estimated that 39% to 49% of the world's population (2.8–3.5 billion people) are overweight or obese (Powell-Wiley *et al.,* 2021). The incidence of obesity has risen markedly worldwide in the last two decades including Nigeria and it is said to be increasingly replacing the more traditional causes of ill health, such as undernourishment and infectious diseases (Kos and Baker, 2005). It has been shown to contribute directly to incident of cardiovascular disease and associated risk factors such as dyslipidemia, type 2 diabetes, hypertension, and sleep disorders (Neeland, 2021) and also reduces life expectancy by 3 to 14 years (Kos and Baker, 2005). Several approach such as behavioral, diet, exercise and drug treatments are currently use to manage obesity, still yet studies have shown that, most people begin to regain weight a few months after treatment, and also some of these drugs have been associated with side effect (NHS, 1997).

Currently there is lack of scientific data on the effect of *B. aethiopum* fruit on BMI as well as lipid profile parameters on HFD induced obese Wistar Rats. Therefore, this work will evaluate the effect of *B. aethiopum* on BMI and lipid profile parameters of high fat diet induced obese Wistar rats.

This present study is aimed at evaluating the role of *B. aethiopum* fruit on obesity (BMI) and lipid profile parameters on high fat diet obese induced Wistar rats. The result of this study is expected to offer recommendations that may be beneficial in monitoring and management of obesity induces disorder using *B. aethiopum* fruit. The aim of this study was to determine the effect of methanolic extract of *B. aethiopum* fruit on BMI and lipid profile parameters of high fat diet induced obese Wistar rats.

MATERIALS AND METHODS

Study Area

This study was carried out in the Department of Haematology, School of Medical Laboratory Science, in collaboration with Faculty of Pharmaceutical Science, Usmanu Danfodiyo University, Sokoto. Sokoto State has a semi-arid climate and vegetation, it is largely Sudan savannah with an annual rainfall between 500 – 1300 mm and temperature ranges between 15^{o}C and over 40^{o}C during warm days (Erhabor *et al*., 2013).

Ethical Clearance

The ethical approval for this study was sought from Department of Pharmacology, Usmanu Danfodiyo University Sokoto, Nigeria. So as to ensure proper handling of experimental Animals with an approval code of PTAC/Ba/(Me)/OT/61-23.

Experimental Animals

The experiment was conducted on Wistar rats weighing approximately 90 g to 105 g obtained from the Animal House of Faculty of Pharmaceutical Sciences Usmanu Danfodiyo University, Sokoto. Handling and use of Animals in this study were in accordance with the guiding principles for research involving animals as recommended by the declaration of Helsinki and the Guiding principles in the care and use of animals (Von Diemen *et al.,* 2006)**.** All the experimental protocols ware in compliance with the Animal Ethics Committee of Usmanu Danfodiyo University, Sokoto, Nigeria.

Acute Toxicity Studies (LD_{50})

Minimal lethal dose (LD_{50}) of methanolic fruits extract of *Borassus aethiopum* was conducted in accordance with lorke's (Lorke, 1983). The study was carried out in two phases using a total of twelves (12) male rats, in the first phase, nine (9) rats were divided in to three (3) groups of three rats each, group 1, 2 and 3, each of this group were orally administered with 10mg/kg, 100 mg/kg and 1000 mg/kg body weight of the extract respectively, to establish the range of dose producing any toxic effect and they were observed frequently for 24hrs for any sign of acute toxicity.

In the second phase of the acute toxicity study, further specific doses (1600, 2900 and 5000 mg/kg b.w) of the extract were administered orally to three (3) rats (one rat per dose) to further determine the correct LD_{50} value. All the animals were observed frequently for 24hrs for sing of toxicity.

Study Design

A total of twenty-five (25) rats were randomly divided into five (5) groups of five (5) rats each, the groups were as follows:

Group A: Non obese control received a standard food and clean water.

Group B: Obese, fed with standard food and 500 mg/kg body weight of methanolic extract of *Borassus aethiopum* fruit orally.

Group C: Obese, fed with standard food and 750 mg/kg body weight of methanolic extract of *Borassus aethiopum* fruit orally.

Group D: Obese, fed with standard food and 1000 mg/kg body weight of methanolic extract of *Borassus aethiopum* fruit orally.

Group E: Obese, control received a standard food and clean water.

The intervention commenced for a period of two (2) weeks.

Plant Material

B. aethiopum fruits were bought from Sokoto Central market, Sokoto state, Nigeria. They ware authenticated by a staff at Faculty of Pharmaceutical Science, Department of Pharmacognosy and Ethanopharmacy Usmanu Danfodiyo University, Sokoto, Nigeria, by comparing them with existing specimen already deposited at the herbarium with a Voucher Number PCG/UDUS/Arec/0001.

Preparation of *Borassus aethiopum* Fruit Extracts

The *Borassus athiopum* fruit was washed with clean water, the outer covering was peeled off, the fleshy middle part (mesocarp) was sliced in to smaller pieces and allowed to air dry under shade, the dry fruit was grinded to powder, 300g of the powdered *Borassus aethiopum* fruit is then soaked in 70% methanol for 72 hours to create the ethanol extract. After 72hrs of soaking, it was filtered with white cloth and Whatman filter paper number one, the filtrate is then concentrated in an oven at 50^{o}C to dryness for 72 hours. The concentrated extract was finally exposed to air to completely dry. The dried extract was covered and stored at room temperature until required (Ahmed and Sani, 2013).

Induction of Obesity

The animals (rats) were divided into six groups, each containing 5 rats, Control group A (Non obese) were fed with a normal pellet diet (NPD), the remaining four groups were fed with a high fat diet (HFD) derived by fortifying normal pallet with margarine (containing high concentration of saturated fat) for 12 weeks (Von Diemen *et al.*, 2006). After a period of 12 weeks, the rats were checked for evidence of obesity by comparing their body mass index with that of the control group as well as their total cholesterol, triglyceride, HDL-cholesterol and LDL-cholesterol levels. Treatment was commenced on all animals in group B, C and D with methanolic fruit extract of *B aethiopum* giving orally, while group F (obese positive control) with normal pallet, all for a period of two (2) weeks.

Determination of BMI

Measurement of Rats Body Weight

The body weight was measured using gravimetric method. In this method, the weight of each rat was measured in gram (g) before and after induction of obesity, and also one week interval during intervention. This was done by placing each rat into container placed on a weighing balance having zeroed the machine (Ochei and Kolhatkar, 2007).

Measurement of Rats Body Length

The body length of the rats was measured before and after induction of obesity, and also after the extract administration on the day of sacrifice. The length of rats was measured from the anus to the tip of the nose in centimeters (Novelli *et al.*, 2007).

Calculation of Body Mass Index

The body mass index of each rat was calculated using the following expression:

Body Mass Index (g/ cm^2) = Body weight (gram)/ body length (cm^2) (Novelli *et al.*, 2007).

Blood Sample Collection and Processing

After fourteen (14) days of extract administration of the experiment, the animals were fasted overnight and anaesthetized with ketamine 0.05 ml and xylazine 0.03 ml intramuscularly. five milliliters (5 ml) of blood samples were collected from the animals through cardiac puncture into clean plan tubes for T-Chol, TG, HLD-Chol and LDL-Chol assay.

Analytical Analysis

Determination of Total Cholesterol

Serum total cholesterol concentration was determine using kit from Agappe Diagnostics Switzerland GmbH, Lot No: 32100039 (Ochei and Kolhatkar, 2007).

Procedure:

Into test tubes labeled blank, standard and test, the flowing reagents were pipetted as follows:

Reagent	Blank	Standard	Test
Working Reagent (mL)	1.0	1.0	1.0
D H_20 (µL)	10	-	-
Standard (µL)	-	10	-
Sample (µL)	-	-	10

The content of each tube was Mixed and incubate at 37^0C for 5 mins. Absorbance was read at 505nm after zeroing with reagent blank.

CALCULATION:

$$\text{Serum Cholesterol (mmol/L)} = \frac{\text{Absorbance of sample}}{\text{Absorbance of standard}} \times 200$$

Determination of Triglyceride Concentration

Serum triglyceride concentration was determine using kit from Agappe Diagnostics Switzerland GmbH, Lot No:32100141 (Ochei and Kolhatkar, 2007).

Procedure

Into test tubes labeled blank, standard and test, the flowing reagents were pipetted as follows:

Reagent	Blank	Standard	Test
Working Reagent (mL)	1.0	1.0	1.0
D H_20 (µL)	10	-	-
Standard	-	10	-
Sample (ml)	-	-	10

The tubes were mixed and incubate at 37^0C for 5 mins. Absorbance was read at 505nm after zeroing with reagent blank.

CALCULATION:

$$\text{Serum Concentration of Triglyceride (mmol/L)} = \frac{\text{Absorbance of sample}}{\text{Absorbance of standard}} \times 200$$

Determination of HDL-Cholesterol Concentration

Serum triglyceride concentration was determine using kit from Agappe Diagnostics Switzerland GmbH, Lot No: 32120037 (Ochei and Kolhatkar, 2007).

Procedure

HDL REAGENT 300 µL

SAMPLE 300 Ml

Mix and centrifuge at 5000rpm for 5minutes

Into test tubes labeled blank, standard and test, the flowing reagents were pipetted as follows:

Reagent	Blank	Standard	Test
Working Reagent (mL)	1.0	1.0	1.0
D H_20 (µL)	10	-	-
Standard (µL)	-	10	-
Sample (µL)	-	-	10

The content of each tube was Mixed and incubate at 37^0C for 5 mins. Absorbance was read at 505nm after zeroing with reagent blank.

CALCULATIONS:

$$\text{Serum HDL-Cholesterol (mmol/L)} = \frac{\text{Absorbance of sample}}{\text{Absorbance of standard}} \times 200$$

LDL cholesterol estimation

LDL cholesterol is calculated by the friedewald equation

LDL cholesterol (mmol/L) = (Total cholesterol- HDL cholesterol) + triglyceride /2.2

Data Analysis

Data generated from this study were analyzed using statistical package for social sciences (SPSS) version 23. Results were expressed as mean ± standard deviation. The body mass index, T-Chol, TG and HDL-Chol were analyzed statistically using one way analysis of variance (ANOVA). Additionally Post Hoc analysis was used to assess the point at which the difference occurs within the group, while the differences was considered significant when P value was less than 0.05 ($p<0.05$).

RESULTS

The result of acute toxicity study LD_{50}. The mean, standard deviation of both the initial and final body mass index (BMI), Total Cholesterol (T-CHOL), Triglycerides (TG), High Density Lipoprotein Cholesterol (HDL-CHOL) and Low-Density Lipoprotein Cholesterol (LDL-CHOL) of all the experimental animal including respective controls in this study were shown in table 1 to 3. The Post Hoc analysis indicating differences between the groups are equally presented.

Table 1: Acute toxicity study (LD_{50}) of Methanolic Fruit Extract of *B. aethiopum* on Wistar Rats.

Table 2: Effect of Methanolic Fruit Extract of *B. aethiopum* on BMI of HFD induced obese rats. The difference in the both the initial and final BMI among the groups was statistically significant p=0.001 and 0.001 respectively. There was a significant increase in the BMI of groups B, C, D, E and F rats when compared with group A rats ($p<0.05$).

Table 3: Effect of Methanolic Fruit Extract of *B. aethiopum* on T-CHOL, TG, HDL-CHOL and LDL-CHOL of HFD induced obese rats. The difference in the both the T-Chol and TG among the groups was found to be statistically significant p=0.000 and 0.000 respectively.

Table 1: Acute toxicity study (LD_{50}) of Methanolic Fruit Extract of *B. aethiopum* on Wistar Rats.

Animals	**Phase 1 N=3**	**Phase 2 N=1**	**Observation**
Group 1	10 mg/kg	1600 mg/kg	No death
Group 2	100 mg/kg	2900 mg/kg	No death
Group 3	1000 mg/kg	5000 mg/kg	No death

The LD_{50} was found to be greater than 5000 mg/kg (> 5000 mg/kg) body weight at the administered dose.

KEY; Phase 1: Day One; Phase 2; Day Two; N: Number of rats in each phase; mg/kg: milligram per kilogram body weight

Table 2: Effect of Methanolic Fruit Extract of *B. aethiopum* on BMI of HFD induced obese Wistar rats

Parameter	Group A (n=5)	Group B (n=5)	Group C (n=5)	Group D (n=5)	Group E (n=5)	P-value
Initial BMI (g/cm^2)	0.58 ± 0.05^a	0.78 ± 0.09^a	0.75 ± 0.06^a	0.80 ± 0.08^a	0.78 ± 0.05^a	0.001
Final BMI (g/cm^2)	0.58 ± 0.05^a	0.75 ± 0.06^b	0.73 ± 0.05^b	0.78 ± 0.05^b	0.75 ± 0.06^b	0.001

Data are expressed as mean ± standard deviation. Values bearing different superscript on the same collum differ significantly ($p\leq0.05$). The difference in both the initial and final BMI among the groups were statistically significant ($p< 0.05$).
KEY; Group A: None obese negative control; Group B: Obese with 500mg of extract; Group C: Obese with 750mg of extract; Group D: Obese with 1000mg of extract; Group E: Obese with 12.5mg of clopidogrel; Group F: Obese positive control; g/cm^2: Gram per centime square and n: Number of rats in each group

Table 3: Effect of Methanolic Fruit Extract of *B. aethiopum* on T-Chol, TG, HDL-Chol and LDL-Chol of HFD induced obese Wistar rats

Parameter	Group A (n=5)	Group B (n=5)	Group C (n=5)	Group D (n=5)	Group F (n=5)	P-value
T-CHOL (mmol/L)	1.5 ± 0.2^a	2.3 ± 0.2^b	1.8 ± 0.5^a	2.4 ± 0.2^b	2.8 ± 0.1^b	0.000
TG (mmol/L)	0.8 ± 0.1^a	1.1 ± 0.1^b	1.1 ± 0.1^b	1.1 ± 0.1^b	1.6 ± 0.1^b	0.000
HDL-CHOL (mmol/L)	0.6 ± 0.1^a	1.1 ± 0.1^b	0.8 ± 0.1^b	1.1 ± 0.1^b	1.0 ± 09^b	0.000
LDL-CHOL (mmol/L)	0.5 ± 0.2^a	0.7 ± 0.2^a	0.57 ± 0.4^a	0.9 ± 0.2^b	1.1 ± 0.1^b	0.001

Data are expressed as mean ± standard deviation. Values bearing different superscript on the same row differ significantly ($p\leq0.05$). The difference in the both the T-Chol, TG, HDL-Chol and LDL-Chol among the groups were found to be statistically significant ($p< 0.05$).
KEY; Group A: None obese negative control; Group B: Obese with 500mg of extract; Group C: Obese with 750mg of extract; Group D: Obese with 1000mg of extract; Group E: Obese with 12.5mg of clopidogrel; Group F: Obese positive control; T-CHOL: Total cholesterol; TG: Triglycerides; HDL-CHOL: High Density Lipoprotein; LDL-CHOL: Low Density Lipoprotein: mmol/L= millimoles per liter and n: Number of rats per group

DISCUSSION

This study was carried out to assess the effect of methanolic extract of *B. aethiopum* fruits on BMI and Lipid profile of high fat diet induced obese Wistar rats, the acute toxicity LD_{50} of the extract was determined, the BMI as well as the T-Chol, TG, HDL-Chol and LDL-Chol in relation to obesity was determined in all the experimental groups including the controls.

Minimal lethal dose of the extract was determined using the method of Lorke (1983), and it was found that, even at a dose of 5000 mg/kg body weight the animals show no sign of toxicity and no mortality, meaning the extract possess no toxic effect by extension safe to consume, this finding is in agreement with the findings of Tata *et al.* (2021); Mohammad *et al.* (2019); Mansur *et al.* (2023) who worked independently and reported no sign of toxicity even at a dose of 5000 mg/kg b.w. through different solvent were use and some previous studies uses the shoot of *B. aethiopum*.

This study shows that, there was a statically significant increase in both the initial and final BMI of groups B, C, D, and E (obese rats) when compared with those of group A rats (non-obese rats) ($p=0.001$), this agrees with work of Speakman *et al.* (2007) that pointed any 20g increase in body weight between negative control (non-obese) and experimental group can be consider as a marker for obesity. Mariana *et al.* (2021) and Novelli *et al.* (2007) also said that, difference in body mass index (BMI) can be considered as a marker of obesity. Like previous studies, high fat diet was used to induce obesity, hence the findings. It was observed that, the BMI of the rats decreases with increasing dose of the extract, indicating the effect of the extract in reducing the body weight and by extension BMI.

On the other hand, T-Chol, TG, HDL-Chol and LDL-Chol levels of the group A rats were compared with that of the obese groups B, C, D, and E and indicated a significant increase in the levels of both T-Chol, TG, HDL-Chol and LDL-Chol from the non-obese group (Group A) ($p<0.05$). Mariana *et al.* (2021) reported that, increase in levels of both T-Chol and TG can be used as a marker for obesity. This present study is also in agreement with the work of Leopoldo *et al.* (2016) who also found an increase in both T-Chol and TG level in obese rats. Akiyama *et al.* also reported and increase level of lipid parameters among HFD induced obese Wistar rats. This confirmed to us that, the rats in group B, C, D, and E were indeed obese. Post Hoc analysis between rats of group A and those of group B, C, D, and E all indicated a significant differences ($p<0.05$), except for group C rats (750 mg of extract) that indicated no differences for T-CHOL most likely indicating the extract inability to lower T-Chol level. The difference in LDL-Chol was not significant among group A, B and C, but differs significantly for group D, and E, indicating the extract ability to reduce the level of LDL-Chol at both 500 mg and 750 mg per body weight.

CONCLUSION

From the findings of this study, the following conclusion was made: The extract is safe for consumption and help to reduce BMI and by extension help to improved lipid profile parameters of HFD induced obese Wistar rats.

RECOMMENDATIONS

1. It is recommended that; Obese patient should consume *B. aethiopum* fruit frequently as it has been shown to have no toxic effect and by extension safe.
2. Similar work should be carried out in human.
3. There is need to carry out more research such as gene expression (molecular) studies on the effect of methanolic fruit extract of *B. aethiopum on BMI and lipid profile*

Conflict of Interest: The authors have declared no conflict of interest.

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