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RESEARCH ARTICLE OPEN ACCESS

Aframomum melegueta seeds ethanol extract reduces food intake, body weight, and hyperglycaemia in high-fat-diet streptozotocin-induced diabetic Wistar rats

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Abstract
Objective: This study investigated the therapeutic potential of *Aframomum melegueta* ethanol seed extract (AMsext) and compared it with the standard drug, metformin, in high-fat-diet streptozotocin-induced type-2 diabetes mellitus (T2DM) Wistar rats.
Methods: Thirty high-fat diet (HFD) streptozotocin-induced T2DM male Wistar rats (FBG >240mg/dl) were randomised into five groups: 1. High-fat-diet normal control (HNC), 2. non-treatment diabetic control (NtDC), and 3. Treatment diabetic groups: 3a = Diabetes +100 mg/kg metformin (Metf), 3b = Diabetes +150 mg/kg AMsext (AMsext150), and 3c = Diabetes +300 mg/kg AMsext (AMsext300). Relative food intake (RFI) was calculated while body weight and fasting blood glucose (FBG) level were determined using standard methods.
Results: Treatment for seven days reduced FBG level in AMsext300 (181.33 ± 63.14, p = 0.004) and Meft (168.00 ± 60.02, p = 0.002) groups compared to NtDC (394.00 ± 67.82). In 14 days, FBG level was reduced in AMsext150 (181.67± 58.62, p = 0.004), AMsext300 (148.00 ± 29.46, p = 0.001) and Metf (112.67±10.60, p = 0.000) compared to NtDC (355.67 ± 64.42). Relative food intake was markedly reduced in AMsext300 (58.51± 20.24, p = 0.024) and Metf (54.29 ± 24.59, p = 0.009) compared to NtDC (98.23 ± 1.21). Rats in the AMsext300 group had 39% greater body weight loss compared to AMsext150 and Metf groups.
Conclusion: AMsext reduced food intake, body weight, and hyperglycaemia in a dose-dependent manner comparable to metformin. Findings validate the ethnnomedicinal and complementary use of *Aframomum melegueta* seeds in the treatment of diabetes mellitus and weight control.

Keywords: *Aframomum melegueta*, Satiety, Diabetes mellitus, Weight loss, Polyphagia

Plain English Summary

Obesity is one of the major causes of disease and death in the world. Being overweight increases the risk of high blood sugar levels. Metformin is the preferred and effective drug used in treating high blood sugar. Some people, when they use metformin, have problems like stomach pain and diarrhoea, resulting in the decision to use native treatment. Alligator pepper (*Aframomum melegueta*) is a plant in the ginger family. It is commonly used in African traditional medicine to treat high blood sugar, yet its claims of lowering blood sugar by users are not well-known.

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This study investigated the blood sugar-lowering effects of *Aframomum melegueta* ethanol seeds extract and compared it with the standard drug, metformin, in high-fat-diet streptozotocin-induced type-2 diabetes mellitus T2DM) Wistar rats.
Results showed that alligator pepper significantly reduced food intake, body weight, and blood sugar level in a dose-dependent manner comparable to metformin. Results from this study support the traditional and complementary use of Alligator pepper in lowering blood sugar levels and body weight control. Findings also provide insights into harnessing the potential of *Aframomum melegueta* for new drug development.

Background

Metabolic syndrome (MetS) is a group of three or more metabolic disorders, which include insulin resistance, hypertriglyceridemia, low high-density lipoprotein (LDL), arterial hypertension, abdominal obesity and impaired fasting blood glucose level (1). MetS, even among children and adolescents, is an emerging public health challenge in low and middle-income countries (2). MetS-related cardiometabolic components are highly prevalent worldwide, having a global prevalence that varied from 12.5% to 31.4% according to the definition considered (3). Overweight/obesity has been associated with about 58% of all individuals with diabetes and 8–41% of people with various types of cancers (4). Obesity is initiated by a positive calorie balance and defined as a body mass index (BMI) ≥30 kg/m^2 in adults (5). It is characterised by insulin resistance, dyslipidaemia, hypertension, and non-alcoholic fatty liver disease (NAFLD) (6, 7).

In 2022, 1 in 8 people in the world were living with obesity, and global adult obesity has more than doubled since 1990, and adolescent obesity has quadrupled. Also, 43% of adults aged 18 years and above were overweight, while 16% were living with obesity; in 2024, 35 million children under the age of 5 were overweight, while over 390 million children and adolescents aged 5–19 years were overweight in 2022, including 160 million who were living with obesity (8). Recent statistics by the World Obesity Atlas revealed that 79% of adults with overweight and obesity will live in Low and Middle-Income Countries (LMICs) by 2035, with the projection that the number of adults living with obesity will rise from 0.81 billion in 2020 to 1.53 billion in 2035 (9). In Nigeria, the estimated prevalence of overweight and obesity was 27.6% and 14.5%, respectively, out of which the southern geopolitical zones had a higher prevalence of overweight/obesity (10). Globally, obesity is one of the major causes of morbidity and mortality, as well as increasing the risk of type-2 diabetes mellitus (T2DM).

Diabetes mellitus (DM) is a chronic disorder of carbohydrate metabolism characterised by hyperglycaemia. DM may be due to absolute or relative deficiency in insulin secretion, insulin resistance, or both (11). Other clinical presentations of DM include polyuria, polyphagia, polydipsia, and weight loss; while complications such as diabetic nephropathy, retinopathy, neuropathy, infection, delayed wound healing, amputation, coma, and death are common in poorly-controlled diabetics, especially in LMICs. Based on aetiologies, DM is classified into three main types: type-1 diabetes mellitus (T1DM), type-2 diabetes mellitus (T2DM), and gestational diabetes mellitus (GDM). Some other rare types of DM include monogenic and secondary diabetes (12, 13). T1DM is also known as insulin-dependent diabetes mellitus (IDDM), which accounts for 5%-10% of people affected with DM. The affected individuals are deficient in insulin secretion from pancreatic beta-cells; hence, they are totally dependent on insulin therapy for survival. T2DM, also known as non-insulin-dependent DM (NDDM), is caused by inadequate insulin secretion and/or insulin resistance. T2DM accounts for about 90% of people suffering from DM. GDM can occur anytime during pregnancy, but generally during the second and third trimesters, accounting for approximately 7% complications of all pregnancies (11). Treatment of DM is based on the type, which usually includes non-pharmacological therapy like modification of lifestyle and diet, moderate physical exercise and/or drugs such as metformin for T2DM. Metformin or 1, 1-dimethylguanidine is a standard and first-line therapy for treatment of T2DM due to its efficacy in glycaemic regulation, low cost and safety profile (14). The anti-diabetic effect of metformin is primarily due to inhibition of hepatic gluconeogenesis, while effects on peripheral and intestinal glucose metabolism are secondary (15). Metformin has been widely used chiefly to treat T2DM until recently, the drug has been repurposed to treat other diseases, including certain neurodegenerative diseases, ageing, cancers, inflammatory diseases and COVID-19 (15, 16, 17, 18). Metformin does not stimulate endogenous insulin secretion; hence, hypoglycaemia or hyperinsulinaemia is a rare side effect compared to other anti-diabetic drugs (19). However, due to genetic polymorphism, reports of observational studies have indicated intestinal side effects in 16% - 62% of patients, resulting in metformin intolerance

in about 5% of patients (20, 21). Consequently, some people have resorted to using medicinal plants as their alternative medicine to treat T2DM. Obesity is the predominant risk factor of T2DM, so body weight remission is an integral strategic approach to achieving effective control of glycaemic level, especially in patients who are both obese and diabetic. Unfortunately, current weight-reducing drugs such as Ozempic and Wegovy are very expensive, thereby limiting their wide usage by most people in LMICs. In addition, Ozempic has been reportedly linked to non-arthritic anterior ischemic optic neuropathy (22, 23). Hence, there is a need to search for safe, effective, and affordable plant-based therapies for T2DM and body weight control.

Aframomum melegueta K. Schum (Alligator pepper) is an herbaceous perennial ethnomedicinal plant; a member of the ginger family, Zingiberaceae. It originates from West Africa and is abundant in Nigeria, Ghana, Togo, Liberia, and the Ivory Coast (24). In Nigeria, *Aframomum melegueta* seeds have different names such as *Ntokon Ibok* (in Efik), *Chitta* (Hausa), and *Atare* (Yoruba). *A. melegueta* has traditional, social, economic, spicy, and medicinal values. Traditionally, the seeds have been used in concoctions to treat different ailments, including cough, body pains, sore throat, diarrhoea, rheumatism, and catarrh (25). In ethnomedicine, the medicinal potentials of flora or fauna depend on their specific functional components or phytochemicals. *A. melegueta* seeds have unique phytochemicals including 6-Gingerol, 8-Gingerol, and Methyl-6-Gingerol, 6-Shogerol, Rac-6-Dihydropardpl, 6-Gingeredione, 2-(5-butyl furan-2yl) ethyl}-2-methoxyphenol, Oleanolic, and acarbase (25). These bioactive compounds have been shown to exhibit hepato-protective, anti-microbial, anti-cancer, and glucose-lowering effects, and fat-mass control (26, 27, 28, 29).

In metabolic disorders, many previous works done on *A. melegueta* seeds extract using different extraction solvents focused much on anti-dyslipidaemic and anti-diabetic potentials. However, the claim of the weight-reducing effect of *A. melegueta* seeds is underexplored. The present study aimed to investigate the impacts of *Aframomum melegueta* ethanol seed extract on satiety, body weight and glycaemic level in high-fat-diet streptozotocin-induced type-2 diabetes Wistar rats.

Materials and Methods

Collection and preparation of Aframomum melegueta ethanol seed extract

Aframomum melegueta dry fruits were purchased in Odo Oba market, in Iwo, Osun state, Nigeria. An amount of 45 g of the seeds was pulverised in a Kenwood Blender and extracted using 1000 ml of 80% ethanol in a conical glass flask (2000 ml) for 72 hours at room temperature by a maceration method. The mixture was agitated twice daily. It was filtered using Whatman filter paper (No. 1) and evaporated using a rotary evaporator and then lyophilised to a 'tar-like' extract labelled as *Aframomum melegueta* seeds ethanol extract (AMsext), stored frozen and used for the study.

Animal Protocol for Experimental Animals and Care

Male Wistar rats aged 5-6 weeks were bred in the Animal House, Medical Laboratory Science Department, Bowen University, Iwo, Osun State. The animals were housed (n = 5) in the standard polypropylene rat cages (410x282x153). Diurnal cycle and temperature (23 ± 2 °C) of the animal house were automatically controlled. The animals were fed with standard rat pellets (Well Feed) and clean water *ad libitum* during the experiment.

Acute toxicity studies of AMsext

Lethal dose (LD_{50}) was carried out using the modified method described by Lorke (30). Nine male Wistar rats were randomised into three groups (1-3) of three rats each. 20 mg/kg, 200 mg/kg and 2000 mg/kg AMsext were administered to groups 1, 2 and 3, respectively. Immediately after administration, it was observed that the animals in groups 2 and 3 either quickly drank water or used their mouths to push the beddings, which probably indicate the peppery effect of the extract. The behaviour lasted between 1 and 2 minutes. There was no mortality or any major sign of acute injury within the first 4 hours, 24 hours, and 14 days.

Modelling of type-2 diabetes mellitus (T2DM)

Sixty male Wistar rats aged 5-6 weeks were fed with a high-fat diet (HFD) formulated with *Zea mays* (30%), Soybeans (15%) and butter (55%) for 10 weeks to induce insulin resistance, a key feature of T2DM. Later, hyperglycaemia, a hallmark of diabetes, was also induced in HFD-fed rats by subcutaneously injecting 1 mL streptozotocin (STZ) at a dose of 35mg/kg body weight freshly prepared using citrate buffer (pH: 4.5). A measured volume, 10% glucose solution, was given *ad libitum* within 18 hours to prevent possible mortality due to sudden hypoglycaemia. Eight days afterwards, FBG was determined using a glucometer and a rat with a mean value of three readings greater than

240 mg/dL was considered hyperglycaemic and classified as a T2DM experimental model.

Experimental Design
Thirty-five male Wistar rats were equally randomised into five (1-5) groups:
1. High-fat-diet normal control (HNC): Non-diabetic rats
2. Non-treatment Diabetes Control (NtDC)
3. AMsext150: Diabetes +150 mg/kg body weight AMsext (treatment group)
4. AMsext300: Diabetes + 300 mg/kg body weight AMsext (treatment group)
5. Metf: Diabetes +100 mg/kg body weight Metformin* (treatment group)
* = A standard drug used to treat T2DM

Determination of body weight and relative food intake (RFI)
During the 14-day treatment period, the body weight of rats in each group was measured three times, on Day 0 (initial), Day 7, and Day 14 using a digital weighing balance. Relative food intake was indirectly determined using the devised formula:
RFI (g) = EFG (g) - LOF (g)
Where RFI is the relative food intake measured in grams (g),
EFG is the equal amount of food (100 g) given between 8:00 and 9:00 a.m. daily.
LOF is the leftover food in the feeding trough plus traceable food in the cage, measured in grams between 8:00 and 9:00 a.m. daily.

Determination of fasting blood glucose (FBG) level
FBG level was determined using a glucometer (Kiptrack Blood Glucose Monitoring System). The tail end of the rats was swapped with 70% ethanol, and a little cut was carefully made with a new razor blade. First, the gush of blood was cleaned off, and then the tip of the glucose test strip was allowed to touch the blood. FBG level (in mg/dL) was read after five seconds.

Statistical analysis
Data was analysed using the PASW Statistics, version 18, a statistical package formerly known as SPSS Statistics from SPSS Inc (Chicago, IL, United States of America). One-way analysis of variance and Bonferroni post hoc test were the statistical tools used to compare means among groups; a p-value less than 0.05 ($p < 0.05$) was considered statistically significant. Results were presented as mean ± standard deviation in tables.

Results
Acute Toxicity Study
Administration of AMsext at 2000 mg/kg body weight did not cause mortality or any major sign of acute injury within 4 hours, 24 hours, or even in 14 days. Hence, the LD_{50} of AMsext was greater than 2000 mg/kg.
Table 1 presents the effect of AMsex and Metformin on the food intake pattern of diabetic male Wistar rats treated for 14 days. There were significant variations ($p = 0.001$) in the relative amount of food consumed among the study groups. Post hoc analysis showed marked reductions in food intake in Metf ($p = 0.009$, $p = 0.012$) and AMsext300 ($p = 0.024$, $p = 0.033$) groups compared to NtDC and HNC. Diabetic control rats had the highest food intake (98.23g), which indicates hyperphagia, a clinical presentation of T2DM (Table 1).

Table 1: Effects of AMsext and metformin on body weight and FBG level of male diabetic Wistar rats in 14 days

Treatment	Equal Amount of Food Given (EFG) (g)	Leftover Food (LOF) (g)	Relative Food Intake (RFI) (g)
HNC	100.00	3.05 ±1.51	96.95 ±1.51
NtDC	100.00	1.77 ± 1.21	98.23 ± 1.21
Metf	100.00	45.71 ± 24.59[ab]	54.29 ± 24.59[ab]
AMsext150	100.00	29.43 ± 23.36	70.58 ± 23.36
AMsext300	100.00	41.49 ± 20.24[ab]	58.51 ± 20.24[ab]

Meft = Metformin, AMsext = *Aframomum melegueta* seeds ethanol extract
[a] = significantly different compared to normal control (HNC)
[b] = significantly different compared to diabetic control (NtDC)

Table 2 shows the effects of AMsext and metformin on the body weight and FBG level of male diabetic Wistar rats in 14 days. Before treatment (0 day), diabetic groups (NtDC, Metf, AMsext150, and AMsext300) had significantly elevated ($p = 0.000$, $p = 0.006$, $p = 0.000$, and $p = 0.000$) FBG levels compared to HNC. However, there was no significant difference in body weight and FBG level among the diabetic groups. Treatment for seven days with metformin (100 mg/kg body weight) and

300 mg/kg body weight of AMsext extract significantly lowered (p = 0.002, p = 0.004) FBG level compared to the NtDC group, with mean difference values of 226.00 and 212.16. Body weight was insignificantly different compared to the NtDC group (Table 2).

Upon treatment for 14 days, the treatment groups - Meft, AMsext150, and AMsext300 had significantly lowered (p = 0.000, p = 0.004, and p = 0.001) FBG levels compared to the NtDC group. Body weight was insignificantly different compared to the NtDC group (Table 2).

Table 2: Effects of AMsext and metformin on body weight and FBG level of male diabetic Wistar rats in 14 days

Treatment	Body weight (g)			Glucose (mmol/L)		
	Initial (0 day)	7 days	14 days	Initial	7 days	14 days
HNC	198.10 ± 20.17	200.20 ±18.88	201.57±19.10	93.67 ±7.09	97.00 ± 1.00	92.33 ± 33.02
NtDC	247.03 ± 45.25	229.30 ± 39.41	191.70 ± 32.58	349.67 ± 48.99[a]	394.00 ± 67.82	355.67 ± 64.42
Metf	231.07 ± 75.54	210.50 ± 79.74	208.00 ±81.73	247.33 ± 32.62[c]	168.00 ±60.02[b]	112.67 ±10.60[b]
AMsext150	265.40 ± 42.23	259.03 ± 20.91	252.97± 16.51	339.67 ±12.66[a]	277.00 ± 7.00	181.67± 58.62[b]
AMsext300	253.00 ± 24.55	222.57±15.44	180.27±42.76	308.33 ± 59.65[a]	181.33 ± 63.14[b]	148.00 ±29.46[b]

[a] = significantly elevated compared to HNC
[b] = significantly lowered compared to NtDC

Table 3 shows the weekly percentage difference in body weight and FBG level of diabetic rats treated with AMsext and metformin for 14 days. Metf and AMsext150 groups had 87.9 % and 4.9 % less body weight loss, respectively, while the AMsext300 group had 39.0% greater body weight loss compared to 112.0 % in the NtDC group in the 2nd week than in the 1st week of treatment. Metf and AMsext 300 groups had 30.3% and 73.8%, respectively, less FBG reduction in the 2nd week than in the 1st week (Table 3).

Table 3: Weekly body weight and FBG response to Metformin and AMsext

Treatment	Mean body weight (BW) difference (g)		Difference in BW	% difference in BW
	0 -7days (1st week)	7-14 days (2nd week)		
NtDC	17.74	37.6	-19.86	-112 (Gbwt)
Metf	20.57	2.5	18.07	87.9 (Lbwt)
AMsext150	6.37	6.06	0.31	4.9 (Lbwt)
AMsext300	30.43	42.3	- 11.87	-39.0 (Gbwt)
	Mean FBG (mg/dl) difference		**Difference in FBG**	**% difference in FBG**
	0 -7days (1st week)	7-14 days (2nd week)		
NtDC	44.33	38.33	6	13.54 (Lglu)
Metf	79.33	55.33	24	30.3 (Lglu)
AMsext150	62.67	95.33	-32.66	-52.1 (Gglu)
AMsext300	127	33.33	93.67	73.8 (Lglu)

(Lbwt) = less body weight loss in 2nd week than 1st week
(Gbwt) = greater body weight loss in 2nd week than 1st week
(Lglu) = less FBG reduction in 2nd week than 1st week
(Gglu) = greater FBG reduction in 2nd week than 1st week

Discussion

This study investigated the effects of *Aframomum melegueta* ethanol seed extract (AMsext) on food intake, body weight and glycaemic level in high-fat-diet and streptozotocin-induced type-2 diabetes mellitus (T2DM) in male Wistar rats.

Before treatment, FBG level (>240 mg/dL) was significantly elevated in the diabetic control and treatment groups (Metf100, AMsext150 and AMsext300) compared to HFD-normal control rats, indicating hyperglycaemia, induced by destruction of the pancreatic β-cells by streptozotocin. The diabetic rats also exhibited excessive food intake

(hyperphagia) and weight loss, which are symptoms of diabetes mellitus.

A significant reduction in FBG level in the AMsext300 group treated for seven days compared to the NtDC group shows a significant dose-dependent anti-diabetic effect of the extract. In the AMsext150 group, a 52.1% reduction in FBG level was observed in the 2nd week compared to the 1st week, which is suggestive of a long-duration-dependent effect of the extract at low dose, while a 73.8 % reduction in FBG level in the 2nd week versus the 1st week in the AMsext300 group, which revealed a long-duration-dependent effect of AMsext at high dose. This finding agrees with a study that earlier reported the glucose-lowering effect of *A. melegueta* seed extract (27). This effect may be due to the inhibition of carbohydrate-digesting enzymes, such as α-glycosidase and α-amylase, by 6-gingerol and oleanoic acid present in the extract (27). It could also be due to inhibition of gluconeogenesis, enhanced insulin sensitivity, and slowed gastric emptying, leading to delayed carbohydrate metabolism and intestinal glucose absorption (31). A 4.9% lower body weight loss in the 2nd week compared to the 1st week in the AMsext150 group suggests a low-dose-dependent effect, while a 39.0% greater body weight loss at the end of the 2nd week compared to the 1st week in the AMsext300 group indicates a high-dose-dependent effect of AMsext on body weight.

A dose-dependent significant reduction in relative food intake and body weight in the groups treated with AMsext was comparable with what was observed in the metformin-treated diabetic rats. Several factors, such as malabsorption, gut microbiome, disruption of gut-brain neurohormonal signals, drugs and significant loss of appetite, can lead to weight loss (31). In this present study, the exact mechanisms behind the marked reduction in relative food intake and body weight are not well understood. Nevertheless, it is suggested that AMsext might contain bioactive compound(s), which individually or synergistically enhance the expression of glucagon-like peptide 1 (GLP-1), a gut peptide hormone released from the L-cells of the intestine in response to a meal (31). GLP-1 is involved in glucose homeostasis, appetite and body weight control through neuronal and hormonal signals in the gut-brain axis (32), and mechanisms include delayed gastric emptying and direct effect on the hypothalamus, the control centre of the gut-brain neurohormonal functions (33).

A. *melegueta* seeds extract has potent glucose-lowering phytochemicals, particularly 6-paradol and Oleanolic acid (27), which could be responsible for the significant reduction in FBG level found in the groups treated with AMsext. The anti-diabetic effect was found to be comparable with metformin, a standard drug used to treat T2DM. At a dose of 100 mg/kg body weight, metformin caused significant reductions in food intake, body weight, and FBG level compared to NtDC. These findings are in agreement with (14) and may be attributed to the mechanisms, including inhibition of hepatic gluconeogenesis, changes in gut microbiome composition, intestinal glucose uptake, secretion of growth differentiation factor 15 (GDF15) and glucagon-like peptide-1 (GLP-1) (34, 35, 36). In this present study, 100 mg/kg of metformin was used as an achievable comparable hepatic effect (~50-100 μM) similar to humans taking 1 g of metformin twice daily (37). Both AMsext and metformin exhibit comparable significant reductions in food intake, glycaemic level, and body weight.

Metformin reduces both basal and postprandial glucose levels mainly by suppressing excessive hepatic glucose production and reducing gluconeogenesis. Other mechanisms by which metformin is used to lower post-prandial glucose include rapid glucose uptake and utilisation in peripheral tissues, increased insulin signalling and fatty acid β-oxidation, decrease in fatty acid and triglyceride synthesis, reduced food intake and intestinal glucose absorption (14, 19). Metformin achieves its therapeutic effect mainly by targeting the liver and gut. An *in vitro* study shows that metformin stimulates GDF15 expression and secretion from hepatocytes, while (36) reported a significantly increased intestinal GDF15 expression with no change in hepatic GDF15 expression in oral metformin-treated mice. Clinically, in patients with T2DM, metformin has been shown to enhance GDF15 release, which might facilitate weight loss (20). However, when compared with metformin, it could be inferred that a significant dose-dependent weight loss in the AMsext300 group might be due to food intake and fat-mass-lowering effects of the extract (29).

In all, AMsext reduced polyphagia, body weight, and hyperglycaemia in a dose-dependent manner comparable to metformin. The combined anti-diabetic and appetite-weight-loss effects of the extract are a promise for a new, safe and effective drug development for the treatment of obesity and T2DM.

List of Abbreviations

AMsext: *Aframomum melegueta* ethanol seed extract
DM: Diabetes mellitus

FBG: Fasting plasma glucose
GDF 15: Growth differentiation factor 15
GLP-1: Glucagon-like peptide 1
HFD: High-fat diet
HNC: High-fat-diet normal control
IDDM: Insulin-dependent diabetes mellitus
LD_{50}: Lethal dose of 50
LMICs: Low and Middle-Income Countries
Metf: Metformin
MetS: Metabolic syndrome
NAFLD: Non-alcoholic fatty liver disease
NDDM: Non-insulin-dependent diabetes mellitus
NtDC: Non-treatment diabetic control
RFI: Relative food intake
STZ: Streptozotocin
T2DM: type-2 diabetes mellitus

Declaration

Ethical approval and consent to participate

This study was approved by the Bowen University Research Ethics Committee (BURG/2023/003) of Bowen University, Iwo, Osun State, Nigeria. The guidelines of the National Institute of Health (38) for the care and use of laboratory animals, and other protocols highlighted by the Bowen University Research Ethics Committee, were strictly followed.

Consent for Publication

All the authors gave consent for the publication.

Availability of data

All data generated or analysed in this study are included in this published article.

Competing interest

The authors declare that they have no competing interests.

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Authors' contributions

FMM and OOA conceived and designed the study. EFU performed the experiment, biochemical and statistical analyses, interpretation of data and wrote the manuscript. DDO did the extraction, experiment, and data collection. OOA also proofread the manuscript. All authors read the final manuscript and approved it for submission.

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