

## Hypolipidemic Effects of Non-Bitter *Cucumis Metuliferus* (Thorn Melon) Fruit Extract in A High-Fat/Fructose Diet and Streptozotocin-Induced Type II Diabetes Mellitus in Wistar Albino Rats

Muriuki Dennis Mwangi<sup>1\*</sup>, Peter Joseph Kasyoki<sup>2</sup>, Atanas Malik Nyabola<sup>3</sup>, Patrick Kubai<sup>4</sup>, Samwel Njagi<sup>5</sup>

<sup>1</sup>Department of Clinical Medicine, Tharaka University, Kenya

<sup>2</sup>Department of Clinical Medicine, Jomo Kenyatta University of Agriculture and Technology

<sup>3</sup>Department of Anatomy, Jomo Kenyatta University of Agriculture and Technology, Kenya

<sup>4</sup>Department of Clinical Medicine, Meru University of Science and Technology, Kenya

<sup>5</sup>Department of Medical Laboratory Sciences, Kenya Medical Training College

\*Corresponding Author Email: [muriukidennis420@gmail.com](mailto:muriukidennis420@gmail.com)

**Accepted: 08 January 2026 || Published: 20 February 2026**

### Abstract

Globally, dyslipidemia remains a lifestyle-associated disease, with ageing and metabolic disorders like diabetes mellitus increasing its risk. The World Health Organization estimates that dyslipidemia is associated with approximately 50% of the global cases of ischemic heart disease, which accounts for over 40% of deaths related to cardiovascular diseases. Today, cardiovascular disease is one of the leading causes of death, accounting for about 31% of worldwide mortality, and is predicted to remain like that in 2030. Although the non-bitter *Cucumis metuliferus* fruit is used by some communities, such as the Kikuyu in Kenya, to manage type 2 diabetes mellitus, its therapeutic benefits have not been adequately studied. The study aimed to determine the effects of non-bitter *Cucumis metuliferus* fruit extract on the lipid profile in Wistar albino rats fed a high-fat/fructose diet and streptozotocin-induced type II diabetes. This study adopted a laboratory-based experimental design. A sample size of 64 male Wistar albino rats, aged 5 weeks and weighing 90 to 130 grams, was randomly assigned to two major study groups: the control and the experimental. The experimental group received a high-fat/fructose diet and a streptozotocin (STZ) injection to induce diabetes mellitus, whereas the control group received a standard rodent pellet diet and 0.9% normal saline. The experimental group was further divided into a positive control group treated with pioglitazone (the standard drug) at 20 mg/kg body weight, a low-dose CMFE group at 200 mg/kg body weight, and a high-dose CMFE group at 400 mg/kg body weight. Serum total cholesterol, triglycerides, low-density lipoprotein, and high-density lipoprotein were measured, and the results were compared between groups. The study findings revealed a significant statistical rise in serum total cholesterol ( $P < 0.001$ ), triglycerides ( $P = 0.019$ ), low-density lipoprotein ( $P = 0.016$ ) and mean total body weight ( $P = 0.033$ ) after treatment with high-fat/fructose diet, which was followed by a decline to levels comparable to the control group after treatment with CMFE and pioglitazone. Similarly, there was a significant decrease ( $P = 0.004$ ) in the beneficial high-density lipoproteins after a substantial high-fat/fructose diet, followed by a significant increase ( $P = 0.001$ ) after CMFE and pioglitazone. This study concludes that the non-bitter *Cucumis*

*metuliferus* fruit extract possesses hypolipidemic properties in type II diabetes mellitus.

**Keywords:** *Cucumis metuliferus*; High fat/Fructose diet; Lipid profile; Streptozotocin; Type II Diabetes

**How to Cite:** Mwangi, M. D., Kasyoki, P. J., Nyabola, A. M., Kubai, P., & Njagi, S. (2026). Hypolipidemic Effects of Non-Bitter *Cucumis Metuliferus* (Thorn Melon) Fruit Extract in A High-Fat/Fructose Diet and Streptozotocin-Induced Type II Diabetes Mellitus in Wistar Albino Rats. *Journal of Medicine, Nursing and Public Health*, 6(1), 26-37.

## 1. Introduction

Dyslipidemia is a metabolic disorder characterized by elevated triglycerides, low-density lipoprotein, and reduced high-density lipoprotein (Warraich & Rana, 2017). It is a common feature of type 2 diabetes mellitus that leads to increased incidences of diabetic complications like neuropathy, retinopathy, nephropathy, and coronary heart disease (Nepalia, 2017). As people age, the prevalence of dyslipidemia in type 2 diabetes increases significantly, and one contributing factor is reduced physical activity (Ahmmed *et al.*, 2021). Insulin resistance in type 2 diabetes mellitus leads to uncontrolled lipid breakdown, causing an influx of non-esterified fatty acids into the liver (Ginsberg *et al.*, 2022). The oversupply stimulates hepatic production of very low-density lipoprotein, initiating a cascade of lipid exchange that increases the risk of cardiovascular morbidity and mortality (Mooradian, 2018). The clinical importance of managing dyslipidemia in type 2 diabetes mellitus cannot be overstated, as cardiovascular disease remains the leading cause of morbidity and mortality. Studies indicate that the risk of coronary heart disease is two to four times higher in diabetics compared to non-diabetics (Rawshani *et al.*, 2018). To lower the risk of cardiovascular complications in type 2 diabetes mellitus, blood sugar control, lipid-lowering, and lifestyle modifications are essential (Jisieike-Onuigbo *et al.*, 2011). Although statin therapy decreases the incidence of dyslipidemia in diabetic patients, thereby lowering the risk of cardiovascular events in type 2 diabetes, this increases the cost of treatment for diabetes mellitus (Rana *et al.*, 2020). *Cucumis metuliferus* has antidiabetic properties, but data supporting its effect on the lipid profile are scarce.

## 2. Material and Methods

### 2.1 Study area

This study was conducted in the Small Animal Facility for Research and Innovation (SAFARI) at Jomo Kenyatta University of Agriculture and Technology (JKUAT) in Kenya.

### 2.2 Study design

A laboratory-based experimental study design was adopted.

### 2.3 Type of animal model used

According to Sood *et al.* (2013), rat disease progression in the Wistar rat model of diabetes mellitus is comparable to that in humans. In this study, Wistar albino rats were used.

#### 2.3.1 Acquisition of Wistar Albino rats

All rats were obtained from the JKUAT SAFARI animal house, where breeding was conducted over 5 generations to establish a pure Wistar Albino colony.

### 2.3.2 Selection of Rats

Five (5) week-old male Wistar albino rats weighing 90 to 130 grams were selected and included in this study.

### 2.3.3 Wistar Albino rats handling

The rats were handled humanely, and the rules and regulations of SAFARI Animal House were adhered to. They were housed in polypropylene rat cages measuring 410 x 285 x 180 mm. The rats were maintained on a 12-hour light/dark cycle and had free access to an approved rodent pellet diet and clean water, as per the experimental protocol.

### 2.4 Sample size calculation

The sample size was arrived at using the "resource equation method" (Charan and Biswas, 2013; Mwangi *et al.*, 2023).

$E = \text{Total number of animals} - \text{Total number of groups}$

$\text{Total number of animals} = \text{No. of animals per group} \times \text{No. of groups}$

$E = (\text{No. of groups} \times \text{No. of animals per group}) - \text{No. of groups}$

E is the degree of freedom of ANOVA, and its value is considered scientifically adequate if it lies between 10 and 20

In this study;

Number of groups = 4

Number of animals per group = 4

Total number of animals = 4 x 4

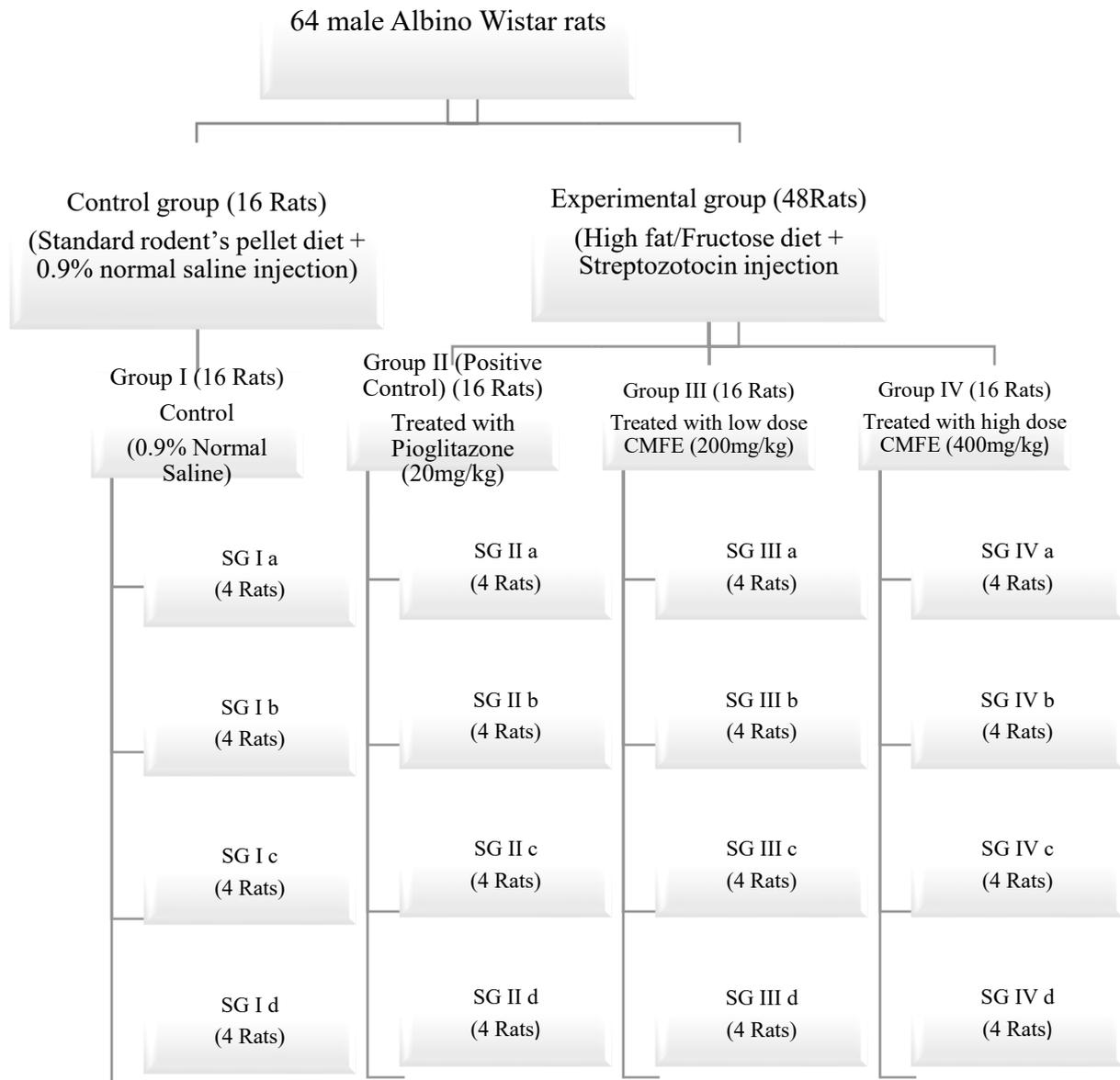
$E = 16 - 4 = 12$

Since the E (12) value was between 10 and 20, the data collected in this study were considered scientifically adequate.

However, the number of animals in each group was multiplied by 4 to cater for the interval of sacrifice on days 45, 56, 63, and 70 of the experiment. This resulted in 16 rats per group, for a total of 64 rats.

### 2.5 Grouping of rats

The Sixty-four (64) male Wistar Albino rats were weighed and randomly assigned into two major groups, i.e., the control and the experimental groups. The experimental group received a high-fat, fructose-containing diet plus a streptozotocin (STZ) injection to induce diabetes mellitus, and the control group received a standard rodent pellet diet plus 0.9% normal saline as a placebo. The experimental group was further divided into treatment group 1 (the positive control group), which was treated with Pioglitazone at a dose of 20mg/kg body weight, treatment group 2, which was treated with low-dose CMFE at 200mg/kg body weight, and treatment group 3, which was treated with high-dose CMFE at 400mg/kg body weight. All the groups had sub-groups "a", "b", c, and "d" each to cater for the serial sacrifice on the 45<sup>th</sup>, 56<sup>th</sup>, 63<sup>rd</sup>, and 70<sup>th</sup> days of the experiment (Figure 1).



**Figure 1: Grouping of animals and treatment**

### 2.6 Harvesting of non-bitter *Cucumis metuliferus* fruit

The non-bitter form of *Cucumis metuliferus* fruits was harvested from a farm in Wamumu ward, Mwea West Sub-County, Kirinyaga County, with the assistance of a plant taxonomist, and subsequently taken to the Department of Botany at Jomo Kenyatta University of Agriculture and Technology for identification and confirmation. A voucher specimen (Voucher No. DMM-JKUATBH 001A-2019) was deposited in the JKUAT botany herbarium for future reference.

### **2.6.1 Extraction of non-bitter *Cucumis metuliferus* crude fruit extracts**

The fruit was extracted by maceration as described by Zhang *et al.* (2018). Whole fruits were washed off dirt and foreign bodies using clean water, and then air-dried. The fruits were then cut in half; the contents were scooped out with a spatula, placed in a collection jar, and then soaked in ethanol in an airtight glass vessel. At room temperature, the mixture was allowed to stand with occasional shaking on an orbital shaker for 48 hours. The liquid was then strained off, and the solid residue was pressed to recover as much of the occluded solution as possible. The liquid was then filtered through muslin cloth and filter paper to remove particles. Ethanol was then evaporated using a rotary evaporator, and freeze-drying was then performed to retain the the *Cucumis metuliferus* fruit extract paste. The paste was stored at 4 degrees Celsius until use.

### **2.7 Preparation of a high-fat and fructose diet for the rats**

In preparing a high-fat diet, the study adopted a protocol developed by Liu *et al.* (2017;Mwangi *et al.* (2023), which states that if more than 35% of a diet's calories come from fat, the diet is considered high in fat. Vegetable cooking fat ('Frymate) manufactured by Pwani Oil Products, Kenya, was mixed with standard rat pellets from Unga Feeds Limited that had the following composition: carbohydrates (65.3%), crude protein (18.1%), crude fibre (7%), fat (8%), calcium (0.8%), and phosphorus (0.8%). Fifteen grams of Frymate (which provided 900 Kcal per 100-gram serving) were mixed with 100 grammes of standard rat pellets, and the mixture was allowed to heat for 15 minutes in a cooking pan placed over an electric cooker set at 50 degrees Celsius. The mixture was stirred during heating for proper mixing and fat penetration into the pellets. The end product gave a composition of carbohydrates (55.5%), fat (21.8%), crude protein (15.4%), crude fibre (6%), calcium (0.7%), and phosphorus (0.7%), making 37% of the calories come from fat. In preparing a fructose diet, this study adopted a protocol developed by Wilson & Islam (2012), which states that rats subjected to 10% fructose solution *ad libitum* before and after treatment with low-dose streptozotocin injection to develop type 2 diabetes had higher chances of survival over eight weeks post-injection than rats fed on a higher fructose amount. A fructose solution was prepared by pouring distilled water into a jar containing 10 grams of fructose while stirring to make a 100-mL solution. The experimental rats had access to the fructose solution *ad libitum* throughout the experiment.

### **2.8 Feeding of the rats**

The control group was fed a standard rat pellet composed of carbohydrates (65.3%), crude protein (18.1%), crude fiber (7%), fat (8%), calcium (0.8%), and phosphorus (0.8%), plus clean water. The experimental group was fed a high-fat diet composed of carbohydrates (55.5%), fat (21.8%), crude protein (15.4%), crude fiber (6%), calcium (0.7%), phosphorus (0.7%), and fructose water. All rats received food and water *ad libitum*.

### **2.9 Confirmation of non-diabetic status before treatment with streptozotocin**

Fasting blood glucose (FBS) and an oral glucose tolerance test (OGTT) were performed to confirm non-diabetic status before streptozotocin treatment to induce diabetes mellitus. The rats were fasted for 6–8 hours in the morning. After fasting, a drop of whole blood was collected via a tail-prick to test for FBS, followed by an OGTT. Rats with FBS <7 mmol/L and OGTT <11.1 mmol/L were included in the study (Patel & Macerollo, 2010).

## 2.10 Reconstitution of streptozotocin (STZ) chemical

Streptozotocin was reconstituted according to the manufacturer's instructions (MedChemExpress, USA), using 0.9% normal saline. After reconstitution, the drug was administered immediately to avoid degradation.

## 2.11 Treatment with streptozotocin to induce diabetes mellitus

STZ treatment was administered on day 42 of the experiment. First, the rats fasted for 6–8 hours in the morning. After fasting, the rats in groups II (positive control), III (low-dose CMFE), and IV (high-dose CMFE) received a single intraperitoneal injection of freshly prepared streptozotocin (40 mg/kg body weight) to induce type II DM. Group I (the control group) received a single intraperitoneal injection of 1 ml of 0.9% normal saline.

## 2.12 Confirmation of diabetes mellitus (DM)

Testing was done on day 45 of the experiment to confirm the presence of DM. First, the rats were fasted for 6–8 hours in the morning, after which a drop of whole blood was collected via a tail prick to test for FBS, followed by an OGTT. Rats with FBS > 7 mmol/L and OGTT > 11.1 mmol/L were considered diabetic and included in the experimental group (Patel & Macerollo, 2010).

## 2.13 Determination of *Cucumis metuliferus* fruit extract dose

According to Jimam et al. (2011), a dose of 1000mg/kg of *Cucumis metuliferus* fruit extract induced liver tissue necrosis and degeneration, whereas the kidneys showed renal epithelial cell damage. However, at a dose of 500mg/kg body weight, there was no significant alteration of liver or renal tissues. The tissues of the spleen and pancreas of rats treated with doses of 500mg/kg and 1000mg/kg of *Cucumis metuliferus* fruit extract were normal. A study by Gotep (2011) showed that diabetic rats treated with 100mg/kg of CMFE had blood sugar levels comparable to those treated with chlorpropamide within 24 hours. Since there was no human data that could be used to calculate the dosage of *Cucumis metuliferus* crude extract, based on the acute oral toxicity study of CMFE conducted before this study and the above references, a dose of 400mg/kg body weight was adopted as the maximum therapeutic dose (high dose) and 200mg/kg body weight as the minimum therapeutic dose (low dose) of CMFE. The low dose was calculated using the natural logarithm function from the highest dose of the crude extract. In this study, the desired potency of the crude extract was 90%.

Least dose = Highest dose  $\times e^{\wedge}$  of 90%

Highest dose=400

$e^{\wedge}$  of 90% =  $1-0.9 = 0.1 = 0.1054$

Least dose =  $400 \times e^{\wedge} (-0.1054) = \text{Approx. } 200$

### 2.13.1 Preparation and administration of the non-bitter *Cucumis metuliferus* fruit extract solution

CMFE paste was reconstituted in 5% DMSO to prepare a 100mg/ml solution of CMFE. The extract was administered at 200mg/kg (low dose) and 400mg/kg (high dose) via oral gavage. Treatment commenced immediately after confirmation of diabetes mellitus on day 45 and continued until day 70 of the experiment.

## **2.14 Determination of pioglitazone dose**

A study by Ogunlana *et al.* (2017) concluded that at doses of 15mg/kg to 45 mg/kg body weight, pioglitazone had no biochemical toxicological effects on Albino Wistar rats. This study used a dose of 20mg/kg of pioglitazone, as described by Chege *et al.* (2019).

### **2.14.1 Preparation and administration of pioglitazone (PGZ) solution**

Pioglitazone solution was prepared by dissolving a 30mg tablet in 5% DMSO to make 6 ml of the mixture. This gave a concentration of 5 mg per 1 ml of the solution. The drug was administered at a dose of 20 mg/kg body weight via oral gavage. Treatment commenced immediately after confirmation of diabetes mellitus on day 45 and continued until day 70 of the experiment.

## **2.15 Humane killing of the rats and collecting tissue specimens**

The humane killing of the rats and collection of tissue specimens were performed in the SAFARI procedure room. First, the rats were fasted for 6–8 hours before being sacrificed. The rat was then placed in a bell jar containing cotton wool, and the jar was sealed. While still covered and via plastic tubing connected to a regulator attached to the gas cylinder, 70% concentrated carbon dioxide was introduced for 1 minute. The anesthesia was allowed to take effect for 3 to 5 minutes, after which the rat was removed from the bell jar and mounted on the board using mounting pins, dorsal side up. Using scissors and forceps, the rat was cut through the ventral medial side from the symphysis pubis to the sternal angle of the thoracic cage, and both intra-thoracic and abdominal structures were exposed for easy access.

A 5-cc syringe with its hypodermic needle was used to collect 4 ml of blood from the heart through direct intracardiac puncture. The blood was emptied into the appropriately labelled collecting test tubes. Blood samples were stored in a refrigerator at 2-8 °C until transport to the biochemistry laboratory for biochemical testing.

A perfusion set was then inserted into the left ventricle, and the remaining blood was cleared by gravity drainage of 200 mL of 0.9% normal saline from the drip set. After sufficient clearing, the saline drip was removed, and, using the same perfusion needle, the desired fixative (10% formalin) was introduced slowly into the rat's circulation. Tail firmness was assessed as an indicator of effective fixation.

## **2.16 Lipid profile testing**

The testing was done according to Kanagasabapathy & Kumari (2000). The collected blood sample was transported to the biochemistry laboratory for processing. The sample was allowed to clot for 15 to 20 minutes, after which it was centrifuged to obtain serum. The CS T240 auto-chemistry analyzer (Dirui Industrial Company Limited) was used to measure serum triglycerides, total cholesterol, low-density lipoprotein (LDL), and high-density lipoprotein (HDL) levels. Reference was made to the laboratory procedure manual from Dirui Industrial Company Limited.

## **2.17 Data analysis**

Quantitative data for total cholesterol, triglycerides, low-density lipoprotein, and high-density lipoprotein were entered into a Microsoft Excel spreadsheet and later transferred to the Statistical Package for the Social Sciences (SPSS) version 25. Means were calculated, and

ANOVA was used to compare multiple means. The Tukey test was used for post hoc analysis. The analysis was conducted at the 95% confidence level ( $P < 0.05$ ). The data was presented in a table.

### 3. Results

#### 3.1 Effects of *Cucumis metuliferus* fruit extract on Lipid Profile

There was a significant statistical increase ( $P = 0.019$ ) in serum triglycerides (TG) between the control group and the treatment groups on day 45 of the experiment, with no significant statistical difference on days 56 ( $P = 0.478$ ), day 63 ( $P = 0.188$ ), and day 70 ( $P = 0.420$ ) of the experiment. Post hoc analysis using the Tukey test revealed a significant increase in serum triglycerides ( $P = 0.019$ ) across all treatment groups on day 45 of the experiment.

There was a significant statistical increase ( $P < 0.001$ ) in total cholesterol (TC) between the control group and the treatment groups on day 45, with no significant statistical difference on days 56 ( $P = 0.180$ ), day 63 ( $P = 0.193$ ), and day 70 ( $P = 0.104$ ) of the experiment. Post hoc analysis using the Tukey test revealed a significant increase in TC ( $P < 0.001$ ) across all treatment groups on day 45 of the experiment.

There was a significant decrease in serum high-density lipoprotein (HDL) in the control group compared with the treatment groups on day 45 ( $P = 0.004$ ), with a significant increase on day 70 ( $P = 0.001$ ). However, there was no statistical difference on days 56 ( $P = 0.671$ ) and 63 ( $P = 0.583$ ) of the experiment. Post hoc analysis using the Tukey test revealed a significant decrease in serum HDL ( $P = 0.004$ ) across all treatment groups on day 45 of the experiment. However, the test also revealed a significant increase in serum HDL in the low-dose CMFE group ( $1.47 \pm 0.58$  test vs.  $1.27 \pm 0.058$  control) and the high-dose CMFE group ( $1.50 \pm 0.100$  test vs.  $1.27 \pm 0.058$  control) on day 70 of the experiment.

There was a significant increase in serum low-density lipoprotein (LDL) cholesterol in the treatment groups compared with the control group on day 45 ( $P = 0.016$ ), with a significant decrease on day 56 ( $P = 0.003$ ). However, there was no significant statistical difference on days 63 ( $P = 0.126$ ) and 70 ( $P = 0.793$ ) of the experiment. Post hoc analysis using the Tukey test revealed a significant increase in serum LDL ( $P = 0.016$ ) across all treatment groups on day 45 of the experiment. A significant drop in serum LDL was observed in the positive control group ( $0.20 \pm 0.100$  test vs.  $0.67 \pm 0.058$  control), low-dose CMFE ( $0.33 \pm 0.153$  test vs.  $0.67 \pm 0.058$  control), and high-dose CMFE ( $0.23 \pm 0.115$  test vs.  $0.67 \pm 0.058$  control) on day 56 of the experiment (Table 1).

An increase in serum triglycerides, total cholesterol, and low-density lipoproteins, and a decrease in serum high-density lipoproteins, in the treatment groups on day 45 of the experiment, could be attributed to a 6-week high-fat and fructose diet administered before STZ-induced type II DM. On the contrary, the decrease in serum triglycerides, total cholesterol, and low-density lipoproteins in the treatment groups to levels comparable to those of the control group, and the increase in serum high-density lipoproteins, confirm that CMFE corrected nutritionally induced dyslipidaemia and prevented diabetic-associated dyslipidaemia.

**Table 1: A table showing results of the effects of non-bitter *Cucumis metuliferus* fruit extract on lipid profile (Expressed in mmol/L)**

|     | Test Day | Control    | Positive Control-PGZ (20mg/kg) | Low Dose CMFE (200mg/kg) | High Dose CMFE (400mg/kg) | F      | p value |
|-----|----------|------------|--------------------------------|--------------------------|---------------------------|--------|---------|
| TG  | 45       | 0.67±0.058 | 1.20±0.300*                    | 1.17±0.115*              | 1.17±0.153*               | 6.051  | 0.019   |
|     | 56       | 0.77±0.153 | 0.90±0.265                     | 0.93±0.145               | 0.67±0.208                | 0.911  | 0.478   |
|     | 63       | 0.70±0.100 | 1.27±0.252                     | 1.13±0.321               | 1.20±0.458                | 2.032  | 0.188   |
|     | 70       | 0.87±0.153 | 1.27±0.306                     | 1.23±0.416               | 1.37±0.503                | 1.055  | 0.420   |
| TC  | 45       | 1.20±0.100 | 2.77±0.153*                    | 2.73±0.208*              | 2.70±0.100*               | 81.487 | <0.001  |
|     | 56       | 1.50±0.108 | 1.40±0.361                     | 1.93±0.416               | 1.53±0.058                | 2.088  | 0.180   |
|     | 63       | 1.57±0.208 | 1.93±0.208                     | 1.73±0.153               | 1.63±0.208                | 2.000  | 0.193   |
|     | 70       | 1.67±0.058 | 2.10±0.361                     | 1.90±0.100               | 1.77±0.580                | 2.871  | 0.104   |
| HDL | 45       | 1.37±0.115 | 0.90±0.100*                    | 0.73±0.208*              | 0.80±0.173*               | 10.161 | 0.004   |
|     | 56       | 1.30±0.100 | 1.10±0.400                     | 1.37±0.379               | 1.37±0.208                | 0.536  | 0.671   |
|     | 63       | 1.17±0.153 | 1.27±0.153                     | 1.30±0.200               | 1.33±0.058                | 0.691  | 0.583   |
|     | 70       | 1.27±0.058 | 1.17±0.058                     | 1.47±0.058*              | 1.50±0.100*               | 15.333 | 0.001   |
| LDL | 45       | 0.60±0.100 | 1.10±0.100*                    | 1.07±0.153*              | 1.07±0.252*               | 6.448  | 0.016   |
|     | 56       | 0.67±0.058 | 0.20±0.100*                    | 0.33±0.153*              | 0.23±0.115*               | 10.911 | 0.003   |
|     | 63       | 0.73±0.153 | 0.50±0.100                     | 0.60±0.173               | 0.47±0.058                | 2.583  | 0.126   |
|     | 70       | 0.70±0.200 | 0.77±0.252                     | 0.83±0.493               | 0.97±0.321                | 0.346  | 0.793   |

Notes: Using one-way ANOVA and Tukey test on post-hoc. \* Indicates significance (p<0.05).

Key: TG=Triglycerides; TC=Total cholesterol; HDL=High density lipoprotein; LDL=Low density lipoprotein

#### 4. Discussion

##### 4.1 Effects of non-bitter *Cucumis metuliferus* fruit extract on lipid profile

Treatment with a high-fat/fructose diet significantly increased serum total cholesterol (TC) (P <0.001), triglycerides (TGs) (P = 0.019), and low-density lipoproteins (LDL) (P = 0.016) on day 45 of the experiment. However, pioglitazone and non-bitter CMFE reduced the parameters to levels comparable to those of the control group on days 63 and 70 of the experiment. On the contrary, treatment with a high-fat/fructose diet significantly decreased (P =0.004) serum high-

density lipoproteins (HDL) on day 45 of the experiment, which was followed by a significant rise ( $P = 0.001$ ) after treatment with non-bitter CMFE, although this was not observed in the PGZ-treated group on day 70 of the experiment, suggesting that non-bitter CMFE is superior to PGZ in the regulation of serum lipids.

The dyslipidemia observed on day 45 of the experiment is consistent with studies by DiNicolantonio and O'Keefe (2018), which demonstrated that prolonged consumption of a high-fat diet causes dyslipidemia in humans. The findings are also consistent with Namekawa *et al.* (2017), who demonstrated that when Wistar rats were fed a high-cholesterol and fructose diet for four (4) weeks, they exhibited signs and symptoms of obesity and hyperglycemia. Udomkasemsab & Prangthip (2019) also demonstrated that a high-fat diet causes dyslipidemia.

While type II diabetes mellitus is associated with an increased risk of developing dyslipidemia, diabetic patients require statin therapy (Daya *et al.*, 2017). This study demonstrates that the non-bitter CMFE may be used to treat diabetic-induced dyslipidemia, thereby reducing the pill burden. Consequently, this lowers the risk of developing cardiovascular complications (Hedayatnia *et al.*, 2020). Although the studies reviewed did not address the extract's hypolipidemic properties, these findings provide new insight into the use of CMFE as a remedy for managing diabetic- and diet-induced dyslipidemia.

## 5. Conclusion

This study concludes that the non-bitter *Cucumis metuliferus* fruit extract possesses hypolipidemic properties, as evidenced by the extract's ability to correct nutrition-induced dyslipidaemia and prevent type II diabetes-induced dyslipidaemia.

## 6. Recommendations

This study recommends the use of non-bitter *Cucumis metuliferus* fruit extract as an adjunct treatment remedy in managing diabetic and nutritionally induced dyslipidaemias.

## 7. Acknowledgement

### 7.1 Funding

None

### 7.2 Ethical approval

Ethical approval (REF: JKU/2/4/896C) was obtained from the JKUAT Animal Ethics Review Committee. Ethical conduct was adhered to at all times during the study. Animals were not used for any purpose other than those specified in the experimental protocol.

### 7.3 Conflict of interest

The authors declare no conflict of interest

## References

- Ahmed, M. S., Shuvo, S. Das, Paul, D. K., Karim, M. R., Kamruzzaman, M., Mahmud, N., Ferdaus, M. J., & Elahi, M. T. (2021). Prevalence of dyslipidemia and associated risk factors among newly diagnosed Type-2 Diabetes Mellitus (T2DM) patients in Kushtia, Bangladesh. *PLOS Global Public Health*, 1(12), e0000003. <https://doi.org/10.1371/journal.pgph.0000003>
- Ginsberg, H. N., Packard, C. J., Chapman, M. J., et al. (2022). Triglyceride-rich lipoproteins

- and their remnants: Metabolic insights, role in atherosclerosis, and emerging therapeutic strategies. *European Heart Journal*, 43(44), 4660-4675.
- Charan, J., & Biswas, T. (2013). How to calculate sample size for different study designs in medical research? *Indian Journal of Psychological Medicine*, 35(2), 121–126. <https://doi.org/10.4103/0253-7176.116232>
- Chege, B. M., Waweru, M. P., Frederick, B., & Nyaga, N. M. (2019). The freeze-dried extracts of *Rothecca myricoides* (Hochst) Steane & Mabb possess hypoglycemic, hypolipidemic and hypoinsulinemic on type 2 diabetes rat model. *Journal of Ethnopharmacology*, 244(July), 112077. <https://doi.org/10.1016/j.jep.2019.112077>
- Daya, R., Bayat, Z., & Raal, F. J. (2017). Prevalence and pattern of dyslipidaemia in type 2 diabetes mellitus patients at a tertiary care hospital. *Journal of Endocrinology, Metabolism and Diabetes of South Africa*, 22(3), 31–35. <https://doi.org/10.1080/16089677.2017.1360064>
- DiNicolantonio, J. J., & O’Keefe, J. H. (2018). Effects of dietary fats on blood lipids: A review of direct comparison trials. *Open Heart*, 5(2), 1–5. <https://doi.org/10.1136/openhrt-2018-000871>
- Hedayatnia, M., Asadi, Z., Zare-Feyzabadi, R., Yaghooti-Khorasani, M., Ghazizadeh, H., Ghaffarian-Zirak, R., Nosrati-Tirkani, A., Mohammadi-Bajgiran, M., Rohban, M., Sadabadi, F., Rahimi, H. R., Ghalandari, M., Ghaffari, M. S., Yousefi, A., Pouresmaeili, E., Besharatlou, M. R., Moohebaty, M., Ferns, G. A., Esmaily, H., & Ghayour-Mobarhan, M. (2020). Dyslipidemia and cardiovascular disease risk among the MASHAD study population. *Lipids in Health and Disease*, 19(1), 1–11. <https://doi.org/10.1186/s12944-020-01204-y>
- Jisieike-Onuigbo, N. N., Unuigbo, E. I., & Oguejiofor, C. O. (2011). Dyslipidemias in type 2 diabetes mellitus patients in Nnewi South-East Nigeria. *Annals of African Medicine*, 10(4), 285–289. <https://doi.org/10.4103/1596-3519.87045>
- Kanagasabapathy, a. S., & Kumari, S. (2000). Guidelines on Standard Operating Procedures for Clinical Chemistry. *World Health Organisation, September*, 1–113.
- Liu, A. G., Ford, N. A., Hu, F. B., Zelman, K. M., Mozaffarian, D., & Kris-Etherton, P. M. (2017). A healthy approach to dietary fats: Understanding the science and taking action to reduce consumer confusion. *Nutrition Journal*, 16(1), 1–15. <https://doi.org/10.1186/s12937-017-0271-4>
- Mooradian, A. D. (2018). Dyslipidemia in type 2 diabetes mellitus. *Nature Reviews Endocrinology*, 14(1), 32-41.
- Mwangi, A. W., Kweri, J. K., Kamau, C. K., Kanyoni, J. M., Kigundu, A. M., Mwangi, E., & Marera, D. (2023). The pregnancy outcomes of female albino rats (*Rattus Norvegicus*) exposed prenatally to varied doses of lamotrigine. *Journal of Agriculture Science & Technology JAGST*, 22(2), 22–33. <https://doi.org/10.4314/jagst.v22i2.3>
- Mwangi, K. J., Kariuki, K. J., Githinji, M. E., Muriithi, K. A., Dominic, M., Wairimu, M. A., & Walter, R. K. (2023). The restorative effects of graded intensities of exercise training on the biochemical and nutritional status of obese induced male Wistar rats (*Rattus*

- novegicus). *Journal of Agriculture, Science and Technology*, 22(3), 39–50.  
<https://doi.org/10.4314/jagst.v22i3.4>
- Namekawa, J., Takagi, Y., Wakabayashi, K., Nakamura, Y., Watanabe, A., Nagakubo, D., Shirai, M., & Asai, F. (2017). Effects of high-fat diet and fructose-rich diet on obesity, dyslipidemia and hyperglycemia in the WBN/Kob-Leprfa rat, a new model of type 2 diabetes mellitus. *The Journal of veterinary medical science*, 79(6), 988–991.  
<https://doi.org/10.1292/jvms.17-0136>
- Nepalia, R. (2017). *Original research article: Role of glycemic control and lipid profiles in management of diabetic complications*. 2(1), 1–4.
- Ogunlana, O. O., Ogunlana, O. E., Ugochukwu, S. K., & Ashano, E. (n.d.). Evaluation of Biochemical Toxicity and Antioxidant Properties of Pioglitazone on Albino Wistar Rats.  
<https://doi.org/10.3923/jms.2017.10.16>
- Patel, P., & Macerollo, A. (2010). Diabetes mellitus: Diagnosis and screening. *American Family Physician*, 81(7), 863–870.
- Rana, J. S., Liu, J. Y., Moffet, H. H., Sanchez, R. J., Khan, I., & Karter, A. J. (2020). Risk of Cardiovascular Events in Patients With Type 2 Diabetes and Metabolic Dyslipidemia Without Prevalent Atherosclerotic Cardiovascular Disease. *American Journal of Medicine*, 133(2), 200–206. <https://doi.org/10.1016/j.amjmed.2019.07.003>
- Rawshani, A., Rawshani, A., Franzén, S., et al. (2018). Risk factors, mortality, and cardiovascular outcomes in patients with type 2 diabetes. *New England Journal of Medicine*, 379(7), 633–644.
- Udomkasemsab, A., & Prangthip, P. (2019). High-fat diet for induced dyslipidemia and cardiac pathological alterations in Wistar rats compared to Sprague Dawley rats. *Clinica e Investigacion En Arteriosclerosis*, 31(2), 56–62.  
<https://doi.org/10.1016/j.arteri.2018.09.004>
- Warraich, H. J., & Rana, J. S. (2017). Dyslipidemia in diabetes mellitus and cardiovascular disease. *Cardiovascular Endocrinology*, 6(1), 27–32.  
<https://doi.org/10.1097/XCE.0000000000000120>
- Zhang, Q. W., Lin, L. G., & Ye, W. C. (2018). Techniques for extraction and isolation of natural products: A comprehensive review. *Chinese Medicine (United Kingdom)*, 13(1), 1–26. <https://doi.org/10.1186/s13020-018-0177-x>