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Antidiabetic Potential of *Vitex mombassae* Fruits Extract in Streptozotocin-Nicotinamide Induced Diabetic Wistar Rat Model

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Abstract

Besides changes in life styles and improper dietary patterns, the rapidly increasing burden of diabetes mellitus type 2 is correlated with antidiabetic agents currently in clinical use, which are costly, less effective, and present undesirable side effects. Natural products from plants are promising alternative sources for developing more effective and cost friendly antidiabetic agents. This study therefore investigated the antidiabetic potential of *Vitex mombassae* fruits extract (VMFE) in streptozotocin-nicotinamide induced diabetic Wistar rat model. Oral acute toxicity test was conducted in male Wistar rat using up and down method by following OECD Guideline 423 (2002). No clinical signs of toxicity were observed at 300 and 2000 mg/kg body weight (b.w.) doses used in the assays. The LD_{50} value was estimated to be > 2000 mg/kg b.w. In evaluation of antidiabetic activity, diabetic Wistar rats were administered with 100, 200 and 300 mg/kg b.w. of VMFE. VMFE resulting into significant lowering of the levels of fasting blood glucose ($p < 0.05$) and increased of level of high-density lipoprotein-cholesterol (HDL-C), levels of total cholesterol (TC), triglyceride (TG) and low-density lipoprotein-cholesterol (LDL-C) were reduced significantly ($p < 0.05$). Therefore, this study provides scientific evidence for antidiabetic activities of *V. mombassae* fruits extracts, and validates its traditional use in the management of diabetes mellitus type 2.

Keywords: *Vitex mombassae*, Diabetes mellitus, Glycemia, Toxicity, Lipid profile.

Introduction

Diabetes mellitus (DM) is a chronic metabolic disease characterized by persistent elevated levels of blood glucose, which over time leads to serious damage to the kidneys, blood vessels, nerves, heart and eyes (Shah et al. 2019). DM is classified into two types namely, diabetes mellitus type 1 (T1DM) and 2 (T2DM). T1DM is caused by destruction of β-cells, which lead to low production of insulin. T2DM is a result of insufficient insulin secretion or insulin resistance (Patel et al. 2012). T2DM is more prevalence than T1DM accounting for about 90% of all diabetes cases in the world (Zheng et al. 2017). According to the International Diabetes Federation (IDF) atlas reports of 2019 and 2021, there has been an increase of 74 million cases of diabetic people (aged 20–79 years) in two years worldwide. Such a

rapid increase has been associated with changes in life styles such as smoking, physical inactivity, and improper dietary patterns (Wanjiru 2018). IDF further estimates that there were 19.8 million cases of people with diabetes in Africa with Tanzania having about 1.7 million cases (Chiwanga et al. 2019). Thus, the increase in the prevalence of diabetes in Africa and indeed Tanzania creates the need for studies that could provide insights for prevention and treatment.

Synthetic antidiabetic drugs are widely used in managing DM; however, they are less effective, and are associated with undesirable side effects such as ketoacidosis and hypoglycemia (Sanchez-Rangel and Inzucchi 2017, Padhi et al. 2020). In this case, therefore, searching for alternative antidiabetic drugs to counteract the challenges is necessary. Some plants have been used in traditional medicine for a long time in treating various ailments and are known to have multiple benefits to patients apart from treating targeted diseases (Ongarora 2021). Such medicinal plants include *Vitex mombassae* Vatke, a small deciduous tree in the family Lamiaceae that grows up to 8 m tall. The plant is widely distributed in tropical African countres including Angola, Botswana, Burundi, DR Congo, Kenya, Malawi, Mozambique, Namibia, Tanzania, Zambia and Zimbabwe. In Tanzania, it is widely found in Mwanza, Tanga, Songea, Iringa, Dodoma and Mbeya regions where it is used traditionally to manage infertility and diabetes (Ruffo et al. 2002). However, its antidiabetic potential has not yet been thoroughly studied. Therefore, this study endeavoured to establish the antidiabetic potential of *V. mombassae* fruits extract in streptozotocin-nicotinamide induced diabetic Wistar rat model.

Materials and Methods

Collection of plant materials

V. mombassae ripened fruits (10 kg) were collected on August 01, 2021 from Haubi village located in Kondoa District (altitude of 1659 m, GPS 4°8'31.4" S and 35°7'48.6" E) and identified by a taxonomist at the Botany Department, University of Dar es Salaam (UDSM). The plant specimen voucher number FMM 4213 was deposited in the herbarium at Botany Department, College of Natural and Applied Sciences, UDSM. The fruits were stored in cool boxes, and transferred to Chemistry Department, UDSM.

Experimental animals

All procedures involving the use of animals in this study followed the guiding principles for animals use in biomedical research provided by the World Medical Association General Assembly (2022) after approval of a protocol by the bioethical committee of UDSM. A total of 80 Wistar rats aged between six and eight weeks weighing 60–120 g were purchased from Sokoine University of Agriculture (SUA). The rats were transported in cages to the Department of Zoology and Wildlife Conservation, UDSM. They were kept in wooden cages in groups of 4 each, for 2 weeks with a supply of food and water *ad libitum* at 28 ± 1.5 ℃ with humidity of 51% at a cycle of 12-hours of dark/light in order to acclimatize to the environment.

Chemicals and reagents

Absolute ethanol from Scharlab S.L., Barcelona-Spain was used for extraction of fruits. Streptozotocin and nicotinamide (from Glentham Life Sciences Ltd, Corsham-United Kingdom) were used to induce T2DM, carboxymethyl cellulose sodium salt (CMC) from Glentham Life Sciences Ltd, Corsham-United Kingdom was used as a suspending agent of the extracts. The kits for aspartate aminotransferase (AST), alanine aminotransferase (ALT), creatinine, high density lipoprotein-cholesterol (HDL-C), triglyceride (TG), and total cholesterol (TC) from Erba Mannheim, Mannheim-Germany were used to measure AST, ALT, creatinine, HDL-C, TG and TC, respectively.

Vitex mombassae fruits extract preparation

The seeds from the fruits of *V. mombassae* were removed and the remaining fresh fruit pulps were shade-dried for 60 days. The samples of gummy dried fruits

were pulverized into fine granules. Then 1000 g of the sample was soaked in 2 L of ethanol twice for 96 hrs, gently shaken every 24 hrs. After filtering through cotton wool and gauze, the extract solution was concentrated at 40 ºC on a rotary vacuum evaporator. A total of 47 g of dry *V. mombassae* fruits extract (VMFE) was obtained and stored in the refrigerator (4–8 ℃) until required for use.

Acute oral toxicity

Acute oral toxicity test was conducted by using a fixed-dose method of up and down in accordance with the Organization for Economic and Cultural Development (OECD) for testing of chemicals no. 423. Nine (9) Wistar rats aged eight to ten weeks weighing between 130–138 g were divided into groups I, II and III each with 3 rats. The rats in each group were marked with a permanent marker of different colours for identification and easy follow-up during observations. After fasting for 12 hrs, the rats in groups I, II and III were weighed and treated as follows: Group I; Wistar rats were administered orally with 1 mL/100 g body weight (b.w.) of 1% carboxymethylcellulose sodium salt (CMC Glentham Life Sciences Ltd) as solvent/negative control, Group II; Wistar rats were administered with VMFE at 300 mg/kg b.w.; and Group III: Wistar rats were administered with VMFE at 2000 mg/kg b.w. suspended in 1% CMC.

Immediately after treatment, the rats were observed for clinical signs of toxicity individually. A close follow-up was made in the first 30 minutes, then after every 30 min in the first 4 hrs. Thereafter, animals were observed after 8 and 12 hrs from the time of administering, and then once daily for 14 days. Food was given to all of the rats 3 hours following the dosage. The clinical signs of toxicity monitored in this experiment included tremors, convulsion, salivation, diarrhoea, sleep, lethargy, coma, fecal state, itching, change in body weight, and death. The body weight was measured on days 0, 7, and 14 using a digital balance. On day 15, the rats were anaesthetized with diethyl ether and sacrificed, then blood was collected in plain evacuating tube with red stoppers by cardiac puncturing. The blood was left to clot at room temperature for 45 minutes, then transferred into 1.5 mL eppendorf tube and centrifuged at 2000 rpm for 15 minutes at 4 ℃ to obtain serum. The serum obtained was used for analysis of the levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT) and creatinine. AST and ALT are important biochemical markers that provide quick diagnosis on the extent of liver damage, and creatinine is a biochemical marker that provide insights on the extent of kidneys damage resulting from toxicity of the test samples.

Determination of aspartate aminotransferase and alanine aminotransferase

The levels of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) in serum were measured by using a UV-Vis spectrophotometer, using Erba's AST and ALT kits, respectively, by following manufacturer's instructions (Chauhan et al. 2018).

Determination of creatinine levels

Creatinine was determined from serum by using Jaffe's modified kinetic method, using Erba's creatinine kits by following manufacturer's instructions (Nirwan and Jain 2017).

Antidiabetic activity

Induction of diabetes mellitus type 2

Induction of T2DM was done as described by Shirwaikar et al. (2004) with modification of dose where Wistar rats aged 8–10 weeks weighing between 130–188 g were fasted for 12 hours, weighed, grouped, and marked permanently. Their fasting glucose levels were recorded using Glucometer-Contour plus-2797 to get baseline data. Nicotinamide dissolved in cold 0.1 M phosphate buffer solution (pH = 7.2) was administered to the rats intraperitoneally at a dose of 120 mg/kg b.w. in order to protect the rats against the severe effects of streptozotocin. After 15 minutes of nicotinamide injection, 60 mg/kg b.w of

streptozotocin dissolved in cold 0.1 M citrate buffer solution (pH = 4.5) was administered intraperitoneally within 20 minutes after preparation. In order to prevent hypoglycaemia-related death, the rats were fed three hours after receiving a streptozotocin injection and allowed free access to a 10 percent sugar solution but not water for 24 hours. To identify the rats that had developed T2DM, the rats were left for 7 days to develop and stabilize the glucose levels, then fasting glucose was measured whereby rats with glucose levels ≥ 10 mmol/L were considered diabetic and selected for this study.

Experimental design

For the purpose of establishing the antidiabetic activities of the test samples, rats were divided into groups. Thus, the diabetic Wistar rats were randomly distributed into 5 groups (groups II–VI) of 3 rats each according to glucose levels. Group I consisted of non-diabetic rats given normal saline, used as normal control. Group II (diabetic rats) given 1% CMC, used as negative control. Groups III given metformin (an antidiabetic drug) 300 mg/kg b.w., was used as a positive control. Groups IV, V and VI were given VMFE at 100, 200 and 300 mg/kg b.w. doses, respectively. The rats received their respective doses once daily and monitored for 21 days. On day 22 the rats were fasted for 12 hrs, anaesthetized by using diethyl ether then humanely sacrificed. Blood was collected in plain evacuating tube with red stoppers through cardiac puncture, which was then allowed to clot at room temperature, then centrifuged at 2000 rpm at 4 ℃ for 15 minutes to obtain serum.

Measurement of body weight and fasting blood glucose level

Body weights and fasting blood glucose (FBG) levels were measured by using digital balance and glucometer, respectively, as described by Ahmed et al. (2010) on days 0, 7, 14 and 21. The formula shown by equation 1 was used to calculate the percentage mean body weight gain.

$$\text{Body weight gain (\%)} = \frac{Bf - Bi}{Bi} \times 100 \quad (1)$$

Where, Bi = initial mean body weight of Wistar rats on day 0; Bf = final mean body weight of Wistar rats on day 21.

Lipid profiling analysis

Total cholesterol (TC), triglycerides (TG) and high density lipoprotein-cholesterol (HDL-C) were measured from serum using UV-Vis spectrophotometer by using Erba's TC, TG and HDL-C kits, respectively, by following manufacturer's instructions as described by Singh et al. (2014). Low-density lipoprotein-cholesterol (LDL-C) was estimated from TC, TG and HDL-C using Friedewald's equation (Friedewald et al. 1972).

Statistical analysis

All data are presented as mean ± standard error of the mean (SEM). One-way analysis of variance (ANOVA) was used to determine if there is any significant difference among different groups (treated and untreated groups) followed by Tukey's post hoc test at $p = 0.05$, the means of the groups with p values ≤ 0.05 were considered statistically different. All the data were analyzed by using Origin Pro 2019b software version 9.65.

Results and Discussion

Results

Acute oral toxicity

Wistar rats exhibited no clinical symptoms of toxicity in response to VMFE, and no deaths occurred at any of the doses examined (Table 1). The symptoms under observations included tremors, convulsions, salivation, diarrhoea, sleep, lethargy, coma, fecal state, itching and death. Statistical analysis revealed a significant difference in the percentage mean weight gain between the control rats and those treated with VMFE at all doses, compared with the untreated rats ($p < 0.05$, Table 2). Also, the extract had no effect on the levels of AST and ALT in the rats (Table 3). In addition, the creatinine levels of treated rats were identical to those of control rats (Table 3). Since there was no death of the animals even at the highest tested dose (Table 1), the median lethal dose (LD_{50})

of VMFE was estimated to be above 2000 mg/kg b.w.

Table 1: Effects of *Vitex mombassae* fruits extract on clinical signs of toxicity in Wistar rats

Physical signs	Tremors	Convulsions	Salivation	Diarrhoea	Sleep	Lethargy	Coma	Fecal state	Itching	Death
Control	N	NS	N	NS	N	NS	NS	N	NS	NS
300 mg/kg VMFE	NS	NS	N	NS	N	NS	NS	N	NS	NS
2000 mg/kg VMFE	NS	NS	N	NS	N	NS	NS	N	NS	NS

N = Normal; NS = Not Seen.

Table 2: Effect of *Vitex mombassae* fruits extract on mean body weight of Wistar rats

Group	Dose	Day 0	Day 14	
		Weight (g)	Weight (g)	Mean weight gain (%)
I	1% CMC	131.98 ± 0.92	160.50 ± 0.50	21.62 ± 0.72
II	300 mg/kg VMFE	135.36 ± 0.43	169.90 ± 1.06	25.51 ± 0.45b
III	2000 mg/kg VMFE	137.25 ± 0.38	175.19 ± 0.40	27.63 ± 0.15b

Data are presented as Mean ± SEM, n = 3. CMC: Carboxymethylcellulose, a = $p > 0.05$ significant difference with respect to the control (1% CMC), b = $p < 0.05$ = significant difference with respect to the control (1% CMC).

Table 3: Effect of *Vitex mombassae* fruits extract on mean ALT, AST and Creatinine levels in Wistar rats

Group	Dose	ALT (IU/L)	AST (IU/L)	Creatinine (mg/dL)
I	1% CMC	15.55 ± 0.84	35.86 ± 0.84	0.11 ± 0.01
II	300 mg/kg VMFE	15.87 ± 0.63a	35.21 ± 0.56a	0.11 ± 0.01a
III	2000 mg/kg VMFE	15.23 ± 0.55a	35.54 ± 0.84a	0.11 ± 0.03a

Data are presented as Mean ± SEM, n = 3. CMC = Carboxymethylcellulose, ALT = Alanine aminotransferase, AST = Aspartate aminotransferase, a = $p > 0.05$ = no significant difference with respect to control (1% CMC).

Antidiabetic activity of *Vitex mombassae* fruits extract

Effects of *Vitex mombassae* fruits extract on fasting blood glucose levels

Mean FBG levels in Wistar rats were 4.1 and 18.9 mmol/L before and after streptozotocin-nicotinamide injection, respectively. The mean FBG levels in the normal control (non-diabetic) rats were significantly lower than those in the negative control diabetic rats, $p < 0.05$ (Figure 1B). Treatment of diabetic rats with VMFE led to concentration-dependent reductions in mean FBG levels (Figure 1) and was significantly reduced in all VMFE-treated groups compared to the negative control group ($p < 0.05$ Figure 1B). Thus, rats treated with 300 mg/kg b.w. metformin and 300 kg/mg b.w. VMFE demonstrated no significant difference in the levels of FBG, $p > 0.05$ (Figure 1B). Although VMFE dramatically lowered the FBG level, it was not comparable to the normal control rats' FBG levels, which were much lower than those of the VMFE-treated rats.

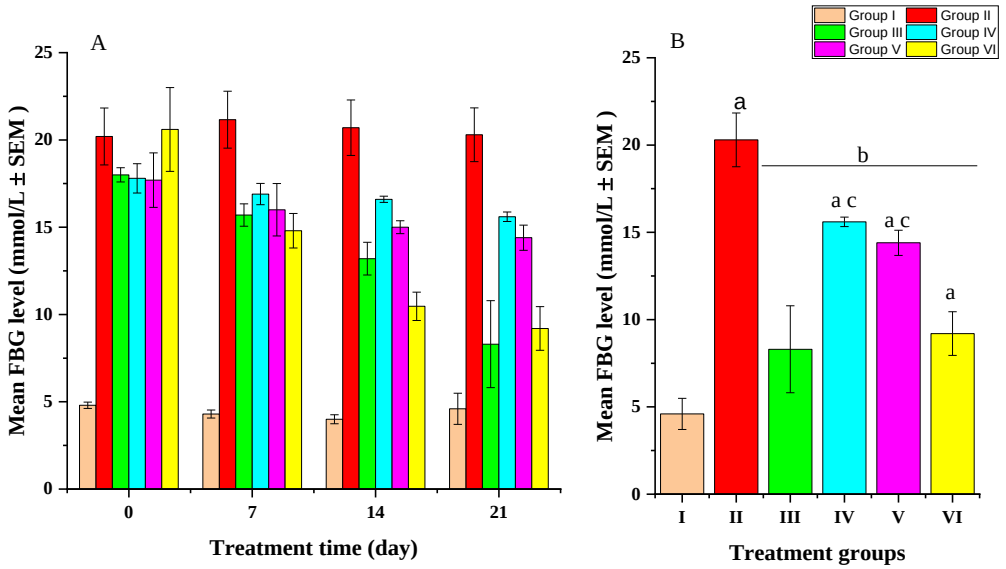

Figure 1: Effects of *Vitex mombassae* fruits extract (VMFE) on fasting blood glucose levels in streptozotocin nicotinamide induced diabetic Wistar rats.

Figure A indicates the trend in fasting blood glucose level from day 0 to 21, and Figure B shows comparison of extract activity on day 21 between control groups with treated groups. Data are presented as mean ± SEM, n = 3. Tukey's multiple comparison test was used to determine p values. a: significant difference with respect to the normal control, b: significant difference with respect to the negative control, c: significant difference with respect to the positive control (metformin) where for all a, b, and c, $p < 0.05$, bars that do not bear letters a, b, and c means no significance difference with respect to the normal control, negative control and positive control, respectively, $p > 0.05$. Group I: Stands for Normal control (non-diabetic rats) given normal saline, Group II: Negative control (diabetic rats) given 1% carboxymethylcellulose, Group III: Positive control (diabetic given standard drug) 300 mg/kg b.w of metformin, Group IV: Diabetic rats given 100 mg/kg b.w. of VMFE, Group V: Diabetic rats given 200 mg/kg b.w. of VMFE, Group VI: Diabetic rats given 300 mg/kg b.w. of VMFE.

Effects of *Vitex mombassae* fruits extract on mean body weight

The effects of *V. mombassae* fruits extract on diabetic rats were also investigated. Thus, Wistar rats were observed to lose weight drastically after nicotinamide and streptozotocin injections. After 21 days of treatment, normal control rats were found to gain the highest percentage body weight, while the negative control (diabetic) were found to lose the highest percentage body weight (Figure 2). Treatment of diabetic Wistar rats with VMFE did not stop body weight loss, but it did slow it down as the dose increased. However, metformin prevented body weight loss resulting in a percentage increase in body weight, in contrast to VMFE (Figure 2).

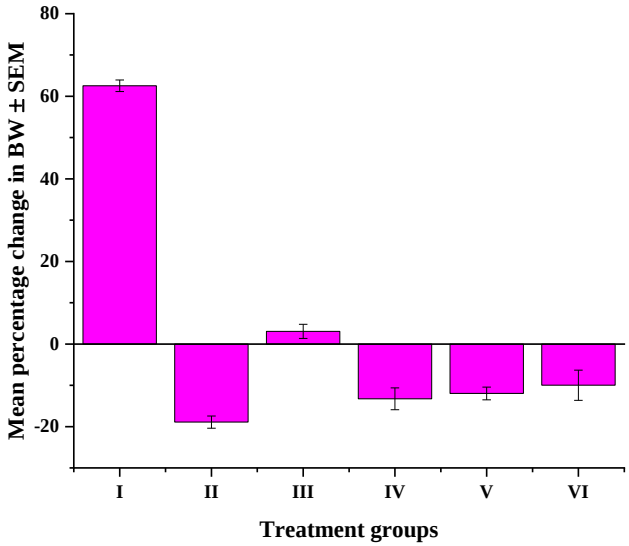

Figure 2: Effects of Vitex mombassae fruits extract on body weight in streptozotocin-nicotinamide induced diabetic Wistar rats.
Data are presented as mean ± SEM, n = 3. Group I: Stands for normal control (non-diabetic rats) given normal saline, Group II: Negative control (diabetic rats) given 1% carboxymethylcellulose, Group III: Positive control (diabetic given standard drug) 300 mg/kg b.w. metformin, Group IV: Diabetic rats given 100 mg/kg b.w. of VMFE, Group V: Diabetic rats given 200 mg/kg b.w. of VMFE, Group VI: Diabetic rats given 300 mg/kg b.w. of VMFE. BW = Body weight.

Effects of *Vitex mombassae* fruits extract on lipid profile

Induction of T2DM in the Wistar rats caused a significant increase in the levels of TC, TG, and LDL-C, and a significant decrease of HDL-C ($p < 0.05$) in comparison to the normal control. In diabetic Wistar rats, VMFE treatment significantly decreased TC, TG, and LDL-C levels while raising HDL-C in a concentration-dependent manner, $p < 0.05$, (Figure 3). VMFE further increased significantly the levels of HDL-C in treated rats than in the negative control rats. The lipid levels were reduced almost back to normal as there was no significant difference between the normal control and the VMFE treated rats.

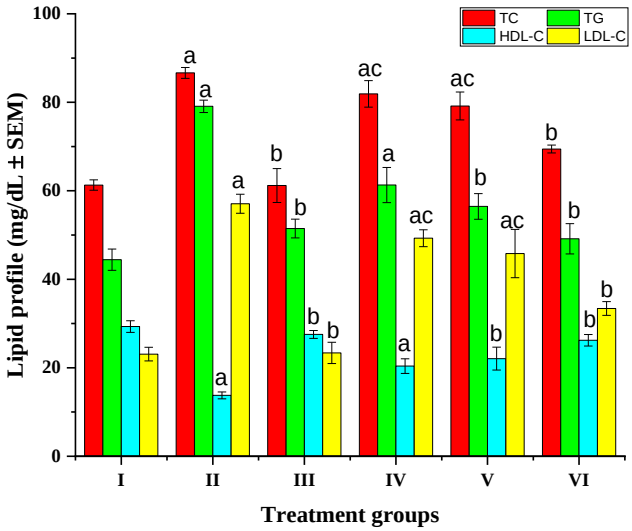

Figure 3: Effects of Vitex mombassae fruits extract on lipid profile levels in streptozotocin-nicotinamide induced diabetic Wistar rats.

Data are presented as mean ± SEM, n = 3. Tukey's multiple comparison test was used to determine *p* values. a = significant difference in comparison to the normal control, b = significant difference in comparison to the negative control, c = significant difference in comparison to the positive control (metformin), where for all a, b, and c, $p < 0.05$, and bar that do not bear letter a, b, and c, are not significantly different with respect to the normal control, negative control, and positive control, respectively, $p > 0.05$. Group I: stands for normal control (non-diabetic rats) given normal saline, Group II: Negative control (diabetic rats) given 1% carboxymethylcellulose, Group III: Positive control (diabetic given standard drug) 300 mg/kg b.w. of metformin, Group IV: Diabetic rats given 100 mg/kg b.w. of VMFE, Group V: Diabetic rats given 200 mg/kg b.w. of VMFE, Group VI: Diabetic rats given 300 mg/kg b.w. of VMFE, TC: Total cholesterol, TG: Triglycerides, HDL-C: High density lipoprotein cholesterol, LDL-C: Low density lipoprotein cholesterol.

Discussion

In this study, *V. mombassae* fruit extract was investigated for its antihyperglycemic effects. This was preceded by evaluation of the toxicity of the extract to the rats. This involved observations of abnormal physical signs on exposure to the extract. Findings, revealed absence of abnormal physical signs. The absence of any aberrant clinical symptoms suggests that VMFE was not hazardous at any of the doses that were examined. The results of this study are consistent with those that Barry et al. (2022) reported for extracts of the leaves of *Vitex doniana* on albino Wistar rats which were found to be non-toxic up to a dosage of 5000 mg/kg body weight, 24 h after treatment and monitoring for fourteen days revealed no any mortality or visible toxic signs.

When animals are exposed to toxins, the body weight tends to decrease. In this study, the fruit extract increased the percentage mean body weight gain in treated rats compared to the control group. These results are similar to those reported by Onwukwe et al. (2020) who investigated toxicity of *V. doniana* leaf extracts on albino Wistar rats and established that *V. doniana* leaf extract increased percentage weight gain in Wistar rats than in control rats. Thus, the increased percentage mean body weight gain could be due to enhanced nutraceutical constituents in

VMFE or enhancement of protein and lipid metabolism probably through increasing the activity of pancreatic lipase, pepsin and trypsin in digestive system thus increasing availability of amino acids, glycerol, and fatty acids for muscle and adipose tissue buildup (Li et al. 2011, Martinez-Gonzalez et al. 2021). In this study, VMFE did not cause significant increase in AST and ALT levels implying it did not cause severe damage to the liver. These findings are similar to those reported for *V. doniana* by Adjei et al. (2021) who found that the extract did not affect the levels of AST and ALT significantly when investigating the toxicity profile of the plant species. Elevated levels of creatinine in the serum are indicators of malfunctioning of kidney (Chebaibi et al. 2019). According to the findings of our study, VMFE did not have an effect on the levels of creatinine, which suggests that it did not damage the kidneys in any way. In addition, LD_{50} value >2000 mg/kg further suggests that VMFE can be tolerable at high dosages and is therefore not harmful to animals.

The toxicity results motivated evaluation of the VMFE for antidiabetic activities by assessing its effects on fasting blood glucose levels in diabetic rats. Thus, VMFE managed to reduce the FBG levels in diabetic Wistar rats indicating its antihyperglycemic activity. The activity of VMFE was comparable to that of metformin at the same dose suggesting that VMFE is as potent as metformin and that it contains bioactive components capable of lowering FBG levels. These results are similar to the findings reported by Nnenna et al. (2020), who investigated the antidiabetic activity of ethanolic extract of *V. doniana* leaf extract in Wistar rats, and found that the extracts of the plants were able to reduce fasting glucose levels in diabetic Wistar rats similar to metformin. The antihyperglycemic activity of VMFE could be highly contributed by synergistic effect of flavonoids, terpenoids, saponins and tannins that have been reported by various studies to be components of the fruits and other parts of the plants in genus *Vitex* (Hamzah et al. 2013, Hu et al. 2017, Berrani et al. 2021). Thus, VMFE could be a potential source of antihyperglycemic agents.

A significant drop in body weight is an indicator of type 2 diabetes (Nasri et al. 2020). In this particular study, a significant reduction in total body weight was detected as an indicator of successful development of type 2 diabetes in the Wistar rats as a consequence of partial insulin insufficiency. Administration of VMFE to diabetic Wistar rats did not prevent the rats from losing weight, as evidenced by the fact that the rats continued to do so to the end of experiment. On the other hand, the pace of weight loss was significantly slower than expected, which suggests that VMFE may have assisted in enhancing the metabolism of carbohydrates, proteins, and lipids. The possible mechanism of action of VMFE could be through its components acting as antioxidants like other species in the genus *Vitex* (Meena et al. 2011), thereby reducing the rate of oxidation of proteins such as enzymes which are involved in metabolism. These findings are akin to those reported by Berrani et al. (2018) on *V. agnus-castus* which also slowed down the rate of weight loss amongst the Wistar rats. This is opposed to the effect of insulin and thiozolidineones which induce weight gain in diabetic patients (Kalsi et al. 2017). Studies show that antidiabetic agents with weight loss effect are preferred than those which facilitate weight gain (Higbea et al. 2017). Since rapid reduction in body weight leads to a low body mass index, which is more preferable for diabetics, VMFE may be an excellent candidate for managing T2DM without leading to an increase in body weight.

Studies shows that production and clearance of lipoproteins in diabetic individuals is interfered by insulin resistance or insufficient insulin leading to high level of triglycerides (TG), low-density lipoprotein-cholesterol (LDL-C), total cholesterol (TC), and low level of high-density lipoprotein-cholesterol (HDL-C) in the blood. High levels of LDL-C and low levels of HDL-C has been linked to high risk of developing coronary heart diseases in diabetic individuals (Gupta et al. 2020). Therefore, a

good antidiabetic agent should not only be able to lower glucose levels but also modulating the lipid profiles. In the current study, the levels of TC, TG, and LDL-C were significantly high, and that of HDL-C significantly low in diabetic Wistar rats in comparison to the normal control. However, treatment of diabetic rats with VMFE decreased the levels of TC, TG and LDL-C and increased HDL-C with the highest dose having higher activity than lower doses. The activity of VMFE at 300 mg/kg b.w. was comparable to metformin suggesting that VMFE can be exploited as an antilipidemic agent. These results are in agreement with those obtained for *V. negundo* (Falguni et al. 2017). The antilipidemic activity of VMFE in lowering the TC, TG and LDL-C may be attributed to ability in stimulating insulin sensitivity in adipose tissues, forming insoluble complexes with cholesterol or their precursor to prevent absorption of TC, increasing the activity of lipoprotein lipase to reduce TG levels, increasing LDL-receptor expression in liver cells to reduce LDL-C and increasing the activity of lecithin-cholesterol acyltransferase (LCAT) to increasing the levels of HDL-C (Sheneni and Idakwoji 2018, Atanu et al. 2021).

Conclusion

The findings of this study show that *V. mombassae* is not toxic at the tested doses, lowered fasting blood glucose levels without causing increase in body weight and was capable of regulating elevated lipid profile in diabetic Wistar rats. This suggests that VMFE is a potential antidiabetic agent. This study reports for the first time a scientifically validated antidiabetic potential of *V. mombassae* using animal model supporting its traditional use in managing diabetes mellitus type 2. However, further investigations need to be conducted to identify the phytochemical constituents present in the plant and evaluate their antidiabetic properties.

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Conflicts of interest

The authors declare that they have no competing interests on this work.

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