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Hypoglycemic, Antihyperlipidemic and Antioxidant Effects of *Manniophyton fulvum* Aqueous Root Extract on Streptozotocin-induced Hyperglycemic Wistar Rats

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Authors' contributions

This work was carried out in collaboration between all authors. Author OEM designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors JCI and AAU managed the analyses of the study. Author SAUO managed the literature searches and interpreted the histology. All authors read and approved the final manuscript.

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Original Research Article

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ABSTRACT

This study investigated the hypoglycemic effect of *M. fulvum* on streptozotocin (STZ)-induced hyperglycemia in Wistar rats. The oxidative damage in the blood, liver, pancreas and kidney cells, hepatic enzyme activities and lipid profile of the Wistar rats were also ascertained. Rats were exposed to STZ alone at 160 mg/kg body weight for one week to induced hyperglycemia before treatment with *M. fulvum* at 83 and 113 mg/kg for 28 consecutive days. Results showed significant elevation in the levels of blood glucose level, amylase activity, serum lipid profile and serum renal markers (total protein, urea and creatinine) in the hyperglycemic rats. Moreover, streptozotocin-

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induced hyperglycemic rats showed significantly ($p < 0.05$) reduced antioxidant status (reduced levels of superoxide dismutase and catalase activities as well as decreased in reduced glutathione and increased level of malondialdehide). *M. fulvum* was able to demonstrate marked hypoglycemic effect and ameliorate the above mentioned biochemical markers. Streptozotocin-induced rats had significant histopathological damages found in the pancreas when compared with the control. The present study shows that *M. fulvum* possesses significant hypoglycemic, antihyperlipidemic and antioxidant effects in streptozotocin-induced hyperglycemic rats due to its ability to effectively reduce or ameliorate the increase in blood glucose levels, lipid profile and oxidative damages.

Keywords: Manniophyton fulvum; streptozotocin; hypoglycemic; hyperglycemic; antihyperlipidemic; antioxidant.

1. INTRODUCTION

Diabetes mellitus developed due to metabolic imbalance which is non-physiological and is characterized by relative or absolute deficiencies in insulin secretion and/or insulin action associated with chronic hyperglycemia and disturbances of carbohydrate, lipid and protein metabolism [1]. It is known worldwide [2] that diabetes mellitus affect about 7% of the adult populations [3] and it is responsible for many deaths globally [4]. The prevalence of diabetes cases is increasing worldwide, especially in the developing countries [5]. Diabetes mellitus is known to cause hyperglycemia that may result in the damage to the eyes, kidneys, blood vessels, nerves and may adversely affect physical, social and psychological well-being of an individual. Some symptoms associated with diabetes mellitus are blurring of vision, weight loss, polyuria, polyphagia and polydipsia. Other serious symptoms of hyperglycemia include non-hyperosmolar coma and ketoacidosis if left untreated [4].

Researchers all over the world are currently working on replacing synthetic anti-diabetic drugs with natural antioxidants from plant materials found in our environment. This may be as a results of new knowledge that diabetes mellitus is associated with the increased free radical formation, decreased antioxidant potential etc. [6]. Research work has also shown that plants contain a large variety of substances that possess antioxidant properties [7,8,9]. This may lead to the formation of advanced glycated end products (AGEs) and other diabetic complications associated with oxidative stress [10].

M. fulvum is one of the important herbs among the common people and local traditional medicine practitioners in African region [11]. It belongs to the family euphorbiacea [12]. In African traditional medicine, the root, stem, bark and leaf are credited with analgesic properties, and are used to treat diarrhea, stomach ache, cough, bronchitis, oxidative stress and inflammation [13]. The red stem sap is credited with hemostatic properties, while the leaf sap is used against ear problems [13]. It is also known as a good treatment option for dysentery and dysmenorrhea [14,15]. The leaf of *M. fulvum* is credited with antioxidant and antidiarrheal properties [16,17].

The Anti-diabetic property of the crude ethanol leave extract of *Manniophyton fulvum* has been studied and the result revealed a dose-dependent reduction in the glucose level after extract administration. The study indicates that the ethanol leave extract of *Manniophyton fulvum* possess antidiabetic activities comparable with the standard drug, metformin [17].

In the present study, the hypoglycemic effect of *M. fulvum* on streptozotocin-induced hyperglycemia, oxidative damage in the blood, liver and kidney cells, hepatic enzyme activities and lipid profile of Wistar rats were evaluated. To evaluate the oxidative damages, the markers such as SOD, CAT activities as well as GSH and MDA levels were determined; to evaluate the effects on the liver, hepatic enzymes AST, ALT and ALP activities were determined; serum lipid profile such as HDL – C, LDL – C, total cholesterol, triglyceride were determined to evaluate the anti-lipidemic effects of *M. fulvum* on streptozotocin-induced rats.

2. MATERIALS AND METHODS

2.1 Chemicals

Streptozotocin, reduced glutathione, bovine serum albumin, glutathione, epinephrine, 5',5'-dithio-bis-2-nitrobenzoic acid (DNTB), bovine serum albumin (BSA), trichloroacetic acid (TCA),

thiobarbituric acid (TBA) and hydrogen peroxide were obtained from Sigma-Aldrich Chemical (St. Louis, MO). Sulfosalicylic acid, di-sodium hydrogen phosphate, sodium di-hydrogen phosphate, and sodium hydroxide were purchased from E. Merck Limited. Total cholesterol, triglycerides, low density lipoprotein (LDL-C), high density lipoprotein (HDL-C) cholesterol levels, aspartate amino transferase, alanine amino transferase, alkaline phosphatase, bilirubin (total and direct), creatinine, urea, and total proteins were estimated from the serum using RANDOX kits. All other reagents were of highest analytical grade and were purchased from the British Drug Houses (Poole, Dorset, UK).

2.2 Animal Husbandry

Fifty adult male Wistar rats (8 weeks old; 130 - 150g) obtained from the Department of Biochemistry, Faculty of Science, University of Port Harcourt, Rivers State, Nigeria were used for the present study. The animals were housed in plastic cages placed in a well-ventilated vivarium and subjected to natural photoperiod of 12-h light:12-h dark cycle. They were fed with rat chow and given drinking water and libitum for two weeks before the commencement of the experiment. All the animals received humane care according to the conditions stated in the 'Guide for the Care and Use of Laboratory Animals' prepared by the National Academy of Science (NAS) and published by the National Institute of Health. The experimental protocols were performed after approval by the University of Port Harcourt Ethical Committee.

2.3 Experimental Design

2.3.1 Streptozotocin-induced hyperglycemia model

Wistar rats were kept in fasting condition for 12 hours, thereafter hyperglycemia was induced by intraperitoneal injection of STZ at 60 mg/kg in freshly prepared PBS in 0.01 M citrate buffer with a pH of 4.3. [18, 19]. After one week, blood samples were obtained by tail prick, and hyperglycemia was confirmed by fasting (8 hours) blood glucose value of 250 mg/dL higher using glucometer (Plusmed).

2.4 Animals Treatment

The rats were randomly divided to five groups of 8 rats each as follows:

Group I (Control): Rats received normal drinking water and feed for 35 consecutive days.
Group II (MF): Rats were orally treated with *M. fulvum* (MF) at the dose of 113 mg/kg body weight, water and feed.
Group III (STZ): Rats were given streptozotocin (STZ) intraperitoneal injection alone at a dose of 60 mg/kg body weight, water and feed.
Group IV (STZ + MF 1): Rats were co-administered with streptozotocin (STZ) intraperitoneal injection at a dose of 60 mg/kg body weight and *M. fulvum* orally at the dose of 85 mg/kg body weight, water and feed.
Group V (STZ + MF 2): Rats were co-administered with streptozotocin (STZ) intraperitoneal injection at a dose of 60 mg/kg body weight and *M. fulvum* orally at the dose of 113 mg/kg body weight, water and feed.
The doses of STZ (60 mg/kg) and MF (85 and 113 mg/kg) used in the present study were chosen based on the results from the pilot study in our laboratory.

2.5 Tissues Sampling

After the induction of diabetes and twenty-four hours after the 28 days treatment, the final body weight of each rat was recorded. Blood samples were collected and kept in plain blood test tubes prior to the animal sacrifice by cervical dislocation. The collected blood samples were centrifuged at 3000 cpm for 10 minutes to obtain the serum, which were thereafter stored at -20^0C before the biochemical assays. The pancreatic tissues were excised, weighed and sent for histological analyses after being washed with ice-cold phosphate-buffered saline.

2.6 Biochemical Assays

The blood glucose concentration was determined using the One Touch ™ glucose strips and glucometer. The serum activities of AST, ALP, ALT and amylase was determined using RANDOX test kits protocol (Randox laboratories, Crumlin, England). Serum levels of conjugated bilirubin, unconjugated bilirubin, total bilirubin, HL – Cholesterol, LL – Cholesterol, total cholesterol, triglyceride, creatinine, urea was also determined using RANDOX test kits protocol (Randox laboratories, Crumlin, England).

2.7 Oxidative Stress Assays

Reduced glutathione (GSH) was estimated by the method of Ellmans [20]. Malondialdehide (MAD) was determined according to the method

described by Ohkawa et al. [21]. Catalase was estimated according to the method of Sinha [22] and superoxide dismutase (SOD) was estimated according to the method of Marklund and Marklund [23].

2.8 Histological Examination

The pancreas collected from 3 rats were fixed in 10% formalin – saline (PBS) solution for twenty – eight (28) at 4°C overnight before they were embedded in paraffin the following day according to the method of Baker and Silverton [24]. In brief, the fixed pancreatic tissues were dehydrated in graded series of alcohol concentrations, cleared by xylene, impregnated in molten paraffin wax and embedded in paraffin wax. The embedded tissues were subsequently cut to produce 5-µm sections using a microtome, fixed on the slides, and stained with hematoxylin and eosin (H&E). Finally, the slides were viewed using the light microscope and histopathological changes were observed and recorded at X 250 magnification.

2.9 Statistical Analysis

Statistical analyses were carried out using one-way analysis of variance (ANOVA) to compare the experimental groups followed by Bonferroni's post-hoc test using GRAPHPAD PRISM 5 software (Version 4; GraphPad Software, La Jolla, California, USA). Values of $p < 0.05$ were considered significant.

3. RESULTS

3.1 Effect of *M. fulvum* Aqueous Root Extract on Fasting Blood Glucose Level of Streptozotocin-induced Hyperglycemic Wistar Rats

The effects of *M. fulvum* on fasting blood glucose level in streptozotocin-induced hyperglycemic rats are presented in Table 1. There was no significant ($p \leq 0.05$) difference in the blood glucose level before hyperglycemia induction. However, there was significant ($p \leq 0.05$) difference in in fasting blood glucose level in STZ alone, STZ + MF 1 and STZ + MF 2 groups when compared with the control. Furthermore, there was significant ($p \leq 0.05$) difference in fasting blood glucose level in STZ alone group when compared with the control. *M. fulvum* treatment significantly ($p \leq 0.05$) reduced fasting blood glucose level in the treated group i.e. STZ + MF 1 and STZ + MF 2 groups. There was also significant ($p \leq 0.05$) difference in fasting blood glucose level in STZ + MF 1 and STZ + MF 2 groups when compared with the STZ alone group.

3.2 Effect of *M. fulvum* Aqueous Root Extract on Amylase Activity of Streptozotocin - induced Hyperglycemic Wistar Rats

The effects of *M. fulvum* on amylase activity in streptozotocin-induced hyperglycemic rats are presented in Fig. 1. There was significant ($p \leq 0.05$) difference in amylase activity in STZ alone when compared to the control. Also, STZ + MF 1 and STZ + MF 2 groups were significantly ($p \leq 0.05$) different when compared with the STZ alone group.

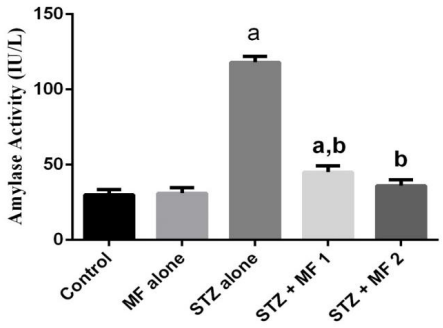

Fig. 1. The effect of *M. fulvum* on streptozotocin-induced hyperglycemic Wistar rats on amylase activity in serum of rat. streptozotocin, STZ; *M. fulvum,* MF; STZ (160 mg/kg body weight); MF 1, (83 mg/kg body weight); MF 2, (113 mg/kg body weight). The data are expressed as mean ± S.D. for 5 rats per group. a: Values differ significantly from control ($p \leq 0.05$). b: Values differ significantly from STZ alone at $p \leq 0.05$

3.3 Effect of *M. fulvum* Aqueous Root Extract on AST, ALP and ALT Activities of Streptozotocin-induced Hyperglycemic Wistar Rats

The effects of *M. fulvum* on liver function markers (AST, ALP and ALT activities) in streptozotocin-induced hyperglycemic rats are presented in Fig. 2. There was significant ($p \leq 0.05$) difference in AST, ALP and ALT activities in STZ alone when compared to the control. Treatment with *M. fulvum* significantly ($p \leq 0.05$) decreased AST,

ALP and ALT activities in the treated group i.e. STZ + MF 1 and STZ + MF 2 groups when compared to the STZ alone group.

3.4 Effect of *M. fulvum* Aqueous Root Extract on Conjugated Bilirubin, Unconjugated Bilirubin and Total Bilirubin Levels of Streptozotocin-induced Hyperglycemic Wistar Rats

The effects of *M. fulvum* on conjugated bilirubin, unconjugated bilirubin and total bilirubin levels in streptozotocin-induced hyperglycemic rats are presented in Fig. 3. There was significant ($p \leq 0.05$) difference in conjugated bilirubin, unconjugated bilirubin and total bilirubin levels in STZ alone when compared to the control. Moreover, treatment with *M. fulvum* for 28 days significantly ($p \leq 0.05$) decreased the levels of conjugated bilirubin, unconjugated bilirubin and total bilirubin in the treated group i.e. STZ + MF 1 and STZ + MF 2 groups when compared to the STZ alone group.

Table 1. Effect of *M. fulvum* aqueous root extract on fasting blood glucose level (mmol/L) of streptozotocin-induced hyperglycemic Wistar rats

Groups	Before induction	After induction	After treatment
Control	4.84±1.34	5.19±1.11	5.16±1.45
MF alone	5.05±1.21	5.07±1.46	4.84±1.34
STZ alone	4.63±1.53	7.25±1.19 [a]	8.87±1.12 [a]
STZ + MF 1	4.84±1.34	7.14±1.09 [a,b]	6.58±1.39 [a,b]
STZ + MF 2	4.96±1.22	7.27±1.17 [a,b]	5.83±1.16 [b]

STZ = streptozotocin, MF = M. fulvum. The data are expressed as Mean ± SD; (n = 5). "a" significantly different from the control at p ≤ 0.05, while "b" significantly different from the STZ alone at p ≤ 0.05

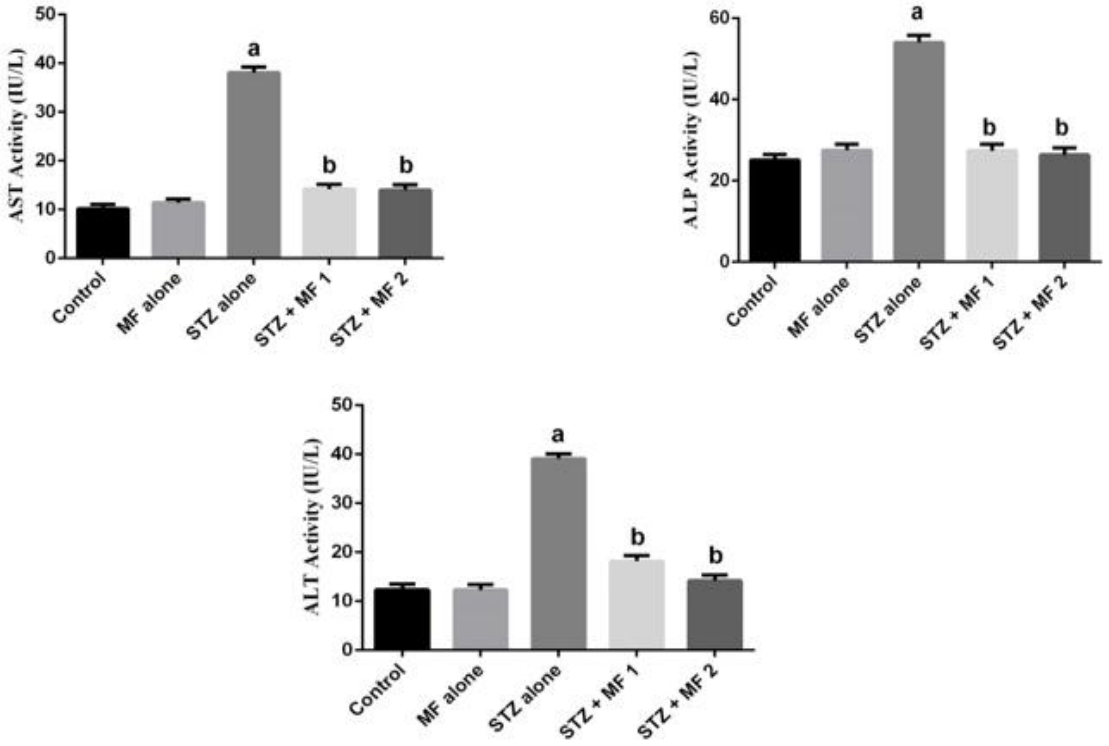

Fig. 2. The effect of *M. fulvum* on streptozotocin-induced hyperglycemic Wistar rats on AST, ALT and ALP activity in serum of rat. streptozotocin, STZ; *M. fulvum,* MF; STZ (160 mg/kg body weight); MF 1, (83 mg/kg body weight); MF 2, (113 mg/kg body weight). The data are expressed as mean ± S.D. for 5 rats per group. a: Values differ significantly from control (p ≤ 0.05). b: Values differ significantly from STZ alone at p ≤ 0.05

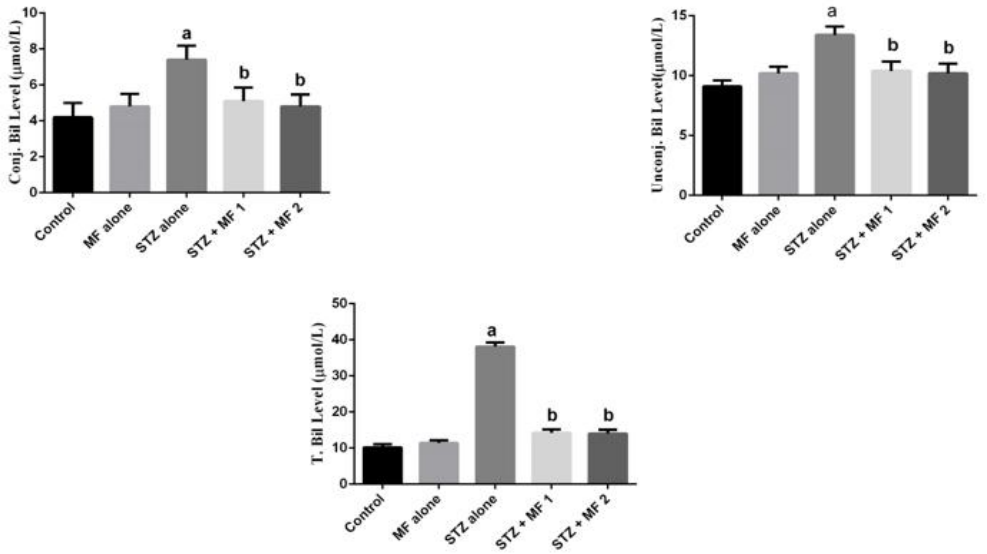

Fig. 3. The effect of *M. fulvum* on streptozotocin-induced hyperglycemic Wistar rats on conjugated bilirubin, unconjugated bilirubin and total bilirubin levels in serum of rat. streptozotocin, STZ; *M. fulvum,* MF; STZ (160 mg/kg body weight); MF 1, (83 mg/kg body weight); MF 2, (113 mg/kg body weight). The data are expressed as mean ± S.D. for 5 rats per group. a: Values differ significantly from control (p ≤ 0.05). b: Values differ significantly from STZ alone at p ≤ 0.05

3.5 Effect of *M. fulvum* Aqueous Root Extract on Cholesterol Levels of Streptozotocin-induced Hyperglycemic Wistar Rats

The effects of *M. fulvum* on HDL – cholesterol, LDL – cholesterol, total cholesterol and triglyceride levels in streptozotocin-induced hyperglycemic rats are presented in Fig. 4. There was significant (p ≤ 0.05) difference in HDL – cholesterol, LDL – cholesterol, total cholesterol and triglyceride levels in STZ alone when compared to the control. But after treatment with *M. fulvum* for 28 days significantly (p ≤ 0.05) decreased the levels of HDL – cholesterol, LDL – cholesterol, total cholesterol and triglyceride in the treated group i.e. STZ + MF 1 and STZ + MF 2 groups when compared to the STZ alone. Furthermore, there was also significant (p ≤ 0.05) difference between STZ + MF 1 and STZ + MF 2 groups when compared to the control group.

3.6 Effect of *M. fulvum* Aqueous Root Extract on Urea and Creatinine Levels of Streptozotocin-induced Diabetic Wistar Rats

The effects of *M. fulvum* on urea and creatinine levels in streptozotocin-induced hyperglycemic rats are presented in Fig. 5. There was significant (p ≤ 0.05) difference in urea and creatinine levels in STZ alone when compared to the control. However, treatment with *M. fulvum* for 28 days significantly (p ≤ 0.05) decreased the levels of urea and creatinine levels in the treated group i.e. STZ + MF 1 and STZ + MF 2 groups when compared to the STZ alone.

3.7 Effect of *M. fulvum* Aqueous Root Extract on Cholesterol Levels of Streptozotocin-induced Hyperglycemic Wistar Rats

The effects of *M. fulvum* on SOD and CAT activities as well as GSH and MDA levels in streptozotocin-induced hyperglycemic rats are presented in Fig. 6. There was significant (p ≤ 0.05) difference in SOD and CAT activities as well as GSH and MDA levels in STZ alone when compared to the control. However, after 28 days treatment with *M. fulvum* significantly (p ≤ 0.05) increased SOD and CAT activities as well as GSH but significantly (p ≤ 0.05) decreased MDA levels in the treated group i.e. STZ + MF 1 and STZ + MF 2 groups when compared to the STZ alone.

3.8 The Effect of *M. fulvum* on Streptozotocin-induced Damages in the Pancreas

The Effect of *M. fulvum* on streptozotocin-induced damages in the pancreas is shown in Fig. 7. Streptozotocin-induced hyperglycemic rats had significant reduction in islet cell mass when compared to the control. However, after treatment with *M. fulvum* i.e. STZ + MF 1 an STZ + MF 2 groups significant increased the islet cell mass when compared with the STZ control group.

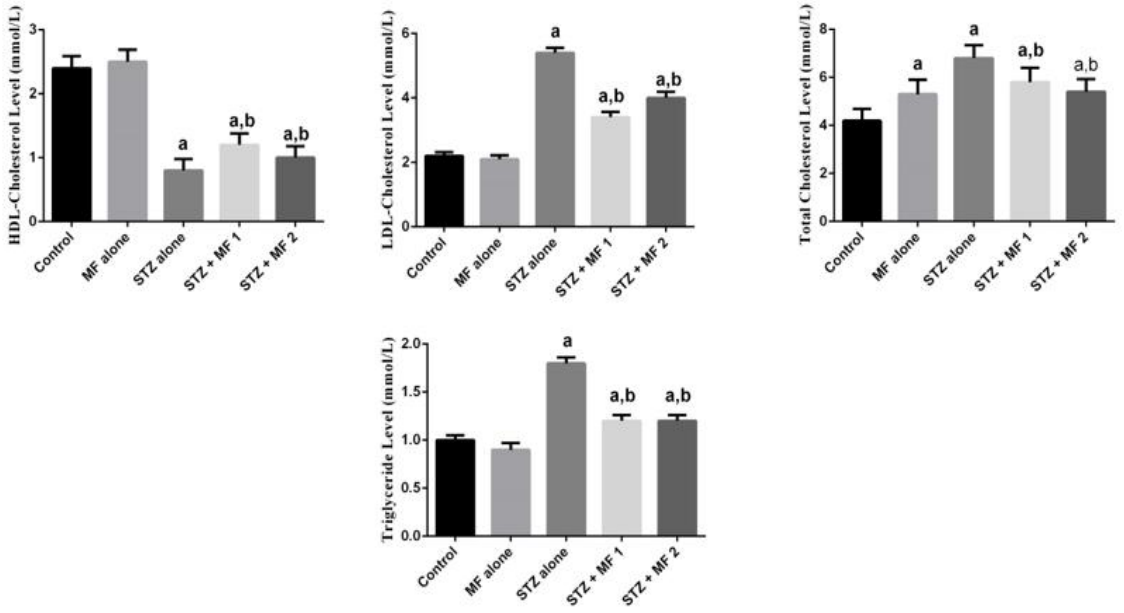

Fig. 4. The effect of *M. fulvum* on streptozotocin – induced hyperglycemic Wistar rats on HDL – C, LDL – C, total cholesterol and triglyceride levels in serum of rat. streptozotocin, STZ; *M. fulvum,* MF; STZ (160 mg/kg body weight); MF 1, (83 mg/kg body weight); MF 2, (113 mg/kg body weight). The data are expressed as mean ± S.D. for 5 rats per group. a: Values differ significantly from control (p ≤ 0.05). b: Values differ significantly from STZ alone at p ≤ 0.05

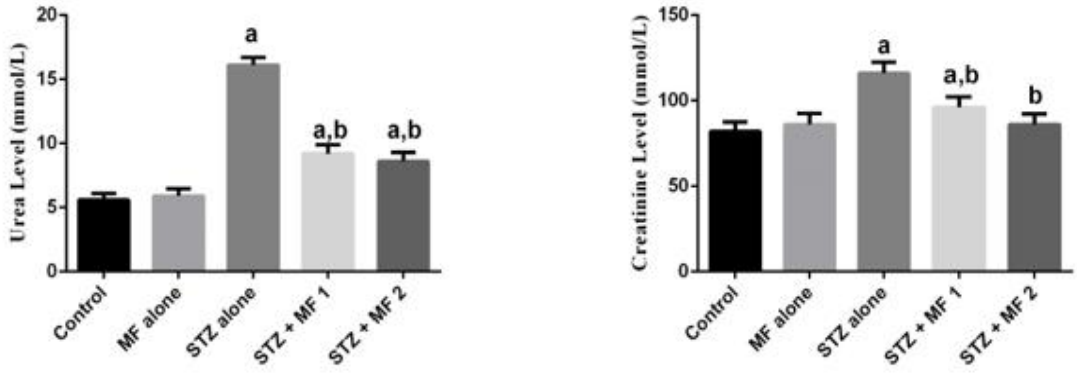

Fig. 5. The effect of *M. fulvum* on streptozotocin – induced hyperglycemic Wistar rats on urea and creatinine levels in serum of rat. streptozotocin, STZ; *M. fulvum,* MF; STZ (160 mg/kg body weight); MF 1, (83 mg/kg body weight); MF 2, (113 mg/kg body weight). The data are expressed as mean ± S.D. for 5 rats per group. a: Values differ significantly from control (p ≤ 0.05). b: Values differ significantly from STZ alone at p ≤ 0.05

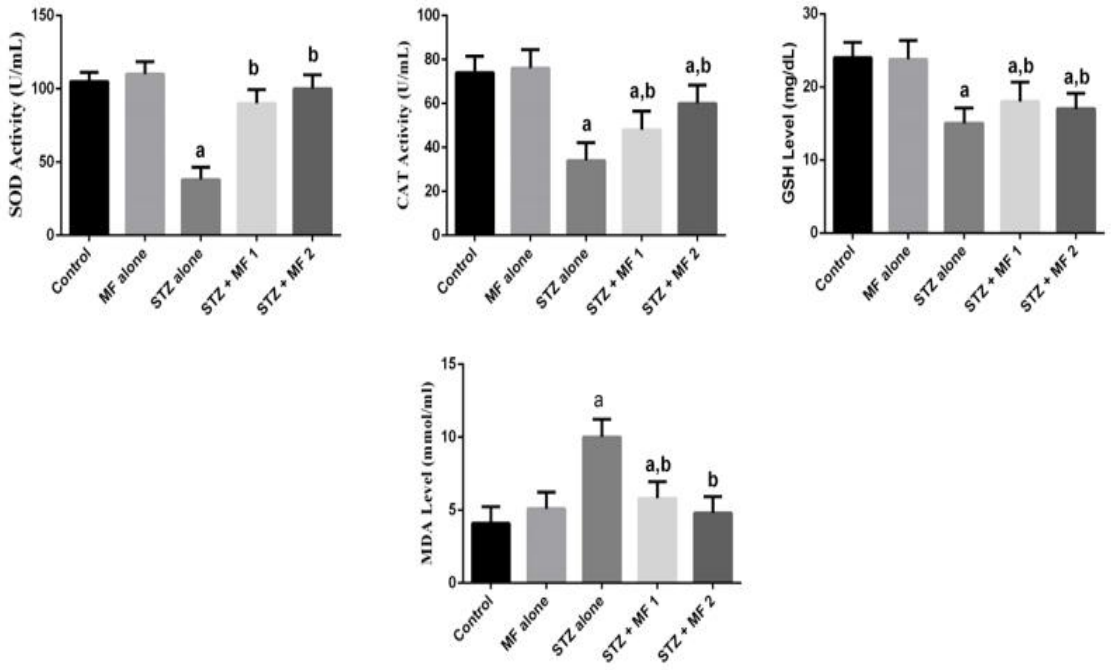

Fig. 6. The effect of *M. fulvum* on streptozotocin-induced hyperglycemic Wistar rats on SOD, CAT activities as well as GSH and M D A levels in serum of rat. streptozotocin, STZ; *M. fulvum,* MF; STZ (160 mg/kg body weight); MF 1, (83 mg/kg body weight); MF 2, (113 mg/kg body weight). The data are expressed as mean ± S.D. for 5 rats per group. a: Values differ significantly from control (p ≤ 0.05). b: Values differ significantly from STZ alone at p ≤ 0.05

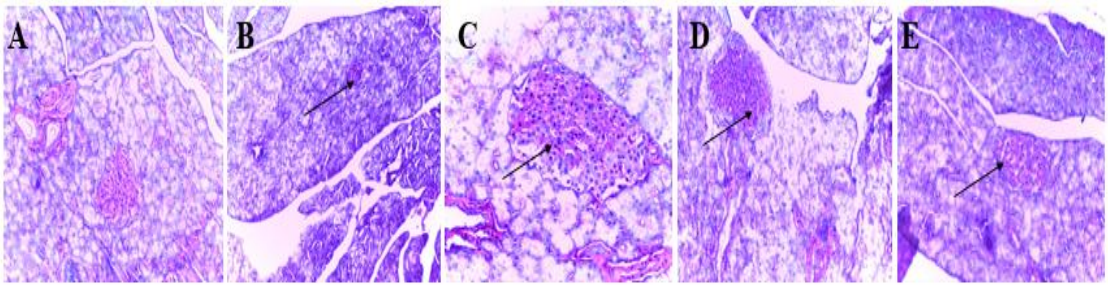

Fig. 7. Representative histopathological sections of the pancreas from the experimental rats. The pancreas of rats from the control (A) and *M. fulvum* alone (B) groups showing normal morphology. The pancreas of rats administered with streptozotocin alone (C) showing marked pancreatic damage. However, the pancreas of rats co-administered with *M. fulvum* at 85 and 113 mg/kg, respectively (D, E) showing normal pancreas and it appeared structurally normal and similar to the control. Magnification of ×250

4. DISCUSSION

In the present study, we investigated the influence of *M. fulvum* against streptozotocin-induced hyperglycemia and its complications in Wistar albino rats. Streptozotocin-induced hyperglycemia has been described by many scientist as a notable experimental model to diabetes mellitus [25,26]. Streptozotocin is known to causes massive reduction in insulin release as a result of the destruction of the β-cells of the islets of Langerhans, thereby resulting in the induction of hyperglycemia experimental model [26]. Free radicals are generated disproportionately in diabetes experimental model [8]. This may

result in the simultaneous decline of antioxidant defense systems which may lead to damage of cellular organelles and enzymes, increased lipid peroxidation, and the subsequent development of insulin resistance. All these complications may promote the development of complications of diabetes mellitus [27].

Several local herbs are being used by the population as alternative therapy for the treatment of diabetes. Most of these herbs have not been subjected to scientific scrutiny to determine their potency. In the present study, we examined the hypoglycemic influence of *M. fulvum* on streptozotocin-induced Wistar rats. Streptozotocin-induced significant increase in fasting blood glucose but *M. fulvum* lowered the fasting blood glucose level to normal in streptozotocin-induced hyperglycemic Wistar rats as also seen in the previous study done with the crude ethanol leave extract [17].

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The pancreas produces amylase which hydrolyses dietary starch into disaccharides and trisaccharides. High concentration of serum level of amylase indicates damage of pancreas. In the present study, streptozotocin-induced hyperglycemic Wistar rats showed significant increase in amylase activity. This implies that streptozotocin may be the cause of the high pancreatic damage as also suggested by previous researches [28, 29]. However, *M fulvum* restored serum amylase activity to normal, indicating that *M. fulvum* ameliorate pancreatic damage induced by streptozotocin.

Liver function enzymes are important markers in diabetic diagnosis and management as it helps to determine the extent of liver damage. In the present study, there was significant increase in the liver function markers in the streptozotocin exposed group. However, *M. fulvum* significantly reduced the liver functions enzymes in the treated groups when compared with the control. The liver plays an important role in glycolysis and gluconeogenesis [30], because it is an insulin dependent tissue, which plays a pivotal role in lipid homeostasis and glucose metabolism. In diabetic condition, the liver is severely affected [31]. In the present study, AST, ALT and ALP enzymes were significant when compared to the control [32]. It has been observed that AST, ALT an ALP enzymes activities in serum of 28 type 1 diabetic patients have elevated enzymes activities [33]. The elevated conjugated and unconjugated bilirubin levels along with increased in total bilirubin observed in streptozotocin-induced rats may be an indication of hepatobiliary damages. However, *M. fulvum* was able to ameliorate the in increased in conjugated and unconjugated and total bilirubin.

M. fulvum treatment reduced serum triglycerides, low-density lipoprotein cholesterol (LDL-c) and fasting blood glucose levels and glucose tolerance, and increased serum high density lipoprotein cholesterol (HDL-c), total cholesterol, and triglyceride. This lipid profile is used to measure hyperlipidaemia which is one of the complications of diabetes. In the present study, there was significant ($p < 0.05$) increase in HDL-C, LDL-C, total cholesterol, and triglyceride in the streptozotocin-induced group (Fig. 4). However, *M. fulvum* was observed to reduce the elevated levels of the serum lipid profile. The elevation of cholesterol in the diabetic control group support the fact that in severe insulin deficiency, there is accelerated lipolysis which result in elevated plasma triacylglycerol level in the diabetic state, as shown by the elevated fasting blood glucose level of same group. *M. fulvum* being a rich protein supplement and antioxidant, it might have antihyperlipidemic activities, thereby resulting in the reduction the rise in serum cholesterol.

Urea and creatinine are nitrogenous end product of metabolism. Urea is the primary metabolite derived from protein turnover while creatinine is the product of muscle catabolism. Elevation of urea and creatinine marks renal failure. Since renal failure is one of the complications of diabetes, the serum levels of urea and creatinine was investigated. Streptozotocin-induced rats show alterations in renal functional markers. There was significant ($p < 0.05$) increase in the renal functional markers (urea and creatinine) of the streptozotocin-induced group (Fig. 5). Similar alternation has been reported in several studies [34,35]. However, *M. fulvum* was observed to reduce the elevated levels of renal functional markers, which has also been reported in several studies [35,4].

The imbalance in pro-oxidants and antioxidants which can result in macromolecular damage (lipid peroxidation) and disruption of redox signalling leads to oxidative stress. The anti-oxidant enzymes (SOD, CAT and GSH) protect major macromolecules in cell from oxidative damage caused by reactive oxygen species

(ROS). SOD catalyses the removal of superoxide radicals to generate hydrogen peroxide (H_2O_2) which in turn is decomposed by catalase (CAT) producing molecular oxygen and water which are not toxic. GSH plays a central role in detoxification and protection against the generation of free radicals thereby maintaining the integrity of cells. In the present study, the streptozotocin-induced oxidative stress (Fig. 6). However, *M. fulvum* significantly increased the plasma activities of superoxide dismutase and catalase, and concentration of reduced glutathione, and reduced significantly the concentration of malondialdehyde. This antioxidant activity may be credited to quercetin present in the aqueous root extract of *M. fulvum*, hence, supporting the previous findings [36, 37]. Streptozotocin-induced rats had significant histopathological damages found in the pancreas when compared with the control. However, *M. fulvum* treatment was able to minimize the pancreatic tissue damages.

5. CONCLUSION

The present study shows that *M. fulvum* possesses significant hypoglycemic, antihyperlipidemic and antioxidant effects in streptozotocin-induced hyperglycemic rats due to its ability to effectively reduced or ameliorate the increase in blood glucose levels, lipid profile and oxidative damages.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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