



Antidiabetic effects of fractions of methanol extract of *Solanum macrocarpon* Linn. On streptozotocin – induced diabetic male Wistar rats

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Abstract

Solanum macrocarpon Linn. (SM) is a well eaten vegetable and prominent for treatment of diseases in folk medicine. This study evaluated the antidiabetic potentials of fractions of methanol extract of *Solanum macrocarpon* in streptozotocin – induced diabetic male Wistar rats.

Diabetes mellitus (DM) was induced in Wistar rats by single (i.p.) dose of 50 mg/kg streptozotocin (STZ) and diabetic rats were administered the extract(s) once daily for four weeks. The effect was determined on body weight (BW), blood glucose concentration (BGC), oral glucose tolerance test (OGGT), hematological indices and lipid profiles. Also, the pancreatic level of oxidative stress and histopathology were determined. Treatment with extracts significantly decreased the elevated BGC, and improved OGTT and BW of diabetic rats. Hematological indices, lipid profiles and pancreatic level of oxidative stress were augmented to near normalcy in diabetic rats administered the extract. Histopathology slides showed improvement in structural integrity of diabetic rats upon treatment with the extracts. The findings of this study have clearly shown that *Solanum macrocarpon* possess antidiabetic ability and could be used in the management of diabetes mellitus.

Keywords Diabetes mellitus · Streptozotocin · *Solanum macrocarpon* · Hematological indices

Introduction

Diabetes mellitus (DM) is an endocrine disorder, persisted with increase in blood glucose as a result of decrease in insulin secretion or inability to utilize the secreted insulin (Karigidi et al. 2020). It is presently a global menace threatening around 500 million people and the number has been predicted to rise to 650 million in 2040 (IDF 2021). This increase may be ascribed to enhanced life expectancy,

consumption of energy rich diet, and physical inactivity of many people, nowadays (Ibrahim et al. 2018). The high blood glucose concentration of diabetic patient always cause disturbance in lipid metabolism and enhanced free radicals production which is the hallmark of hypertension in diabetic patients (Vellapandian and Ramachandram 2022). Certainly, Pancreas being an organ responsible for secretion, storage and utilization of insulin in the body is central to development of DM. One of the prominent causes of pancreas' loss of function is its vulnerability to free radicals attack due to its low antioxidant defense status (Lenzen 2017). Presently, many hypoglycemic drugs with different mechanisms of action have been developed for treatment of DM but there have been many reported shortcomings on them. Because of this, many people still rely on plant-based therapy to treat and manage DM. One of the vegetables used for management/treatment of DM in folk medicine is *Solanum macrocarpon*.

Vegetables are prominent part of human diet because of their richness in protein, micronutrients and vitamins. *Solanum macrocarpon* (SM) belongs to Solanaceae family and

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popularly referred to as African eggplants. It is well cultivated in the tropics because of its numerous uses; the leaves are used as vegetable for soup or herb for treatment of ailments. Its use in preparing soup is due to the fact that it is considered very rich in fibre, zinc, protein, fat and calcium (Komlaga et al. 2014). The leaves are reservoirs of phytochemicals of biological significance (Oyesola et al. 2022). The aqueous extract of the vegetable has been shown to possess antihyperglycemic potential in alloxan-induced DM (Ajiboye et al. 2021).

More than 80% of diabetes burden are carried by low and middle income countries that do not have sufficient financial means to obtain medical care (IDF 2021; Karigidi and Olaiya 2020b). Therefore, they depend on plant-based drugs for treatment and management of DM. Due to this, there is call to scientifically validate some of the plant-based drugs use for treatment of DM. This study is designed to investigate the antidiabetic effects of methanol extract of *Solanum macrocarpon* and its fractions in streptozotocin-induced diabetic male Wistar rats.

Materials and methods

The *Solanum macrocarpon* Linn explored in this study was bought at Bodija market, Ibadan, Nigeria. It was identified and authenticated at Department of Botany, University of Ibadan (UIH-22,543). The leaves were sorted to remove shriveled leaves and washed and dried in the laboratory at ambient temperature for three weeks and milled with electric blender.

Preparation of extract and fractions

The procedure of Karigidi and Olaiya (2020a) was adopted for preparation of extract and fractions.

Animal

Healthy male Wistar rats of 115–120 g weight were bought from the University of Ibadan animal house. They were fed standard pellet diet with and water *ad libitum*. The rats were kept individually in metabolic cage and acclimatized under 12-h light and dark cycle for 14 days prior the induction of experimental DM. The protocol for this study was approved by University of Ibadan, animal care use and research ethics committee for care and use of laboratory animals with reference number (UI-ACUREC/02-0219/21).

Induction of DM

Induction of DM was done as reported by Karigidi and Olaiya (2020a). Rats with fasting blood glucose ≥ 250 mg/dL were used for the study.

Experimental design

After confirmation of DM, the rats were categorized into groups (6) of six rats.

Control: Control rats.

Dcontrol: Diabetic control rats.

SME: Diabetic rats administered SME (300 mg/kg).

ETA: Diabetic rats administered ETA (300 mg/kg).

BUT: Diabetic rats administered BUT (300 mg/kg).

GLIB: Diabetic rats administered Glibenclamide (1 mg/kg).

These extract(s) were administered orally for four weeks with oral gavage. Body weight and blood glucose level were measured every week during the experiment. After four weeks, the rats were euthanized.

Oral glucose tolerance test (OGTT)

On the 27th day of treatment, OGTT was measured as described by Karigidi and Olaiya (2020a).

Heamatological indices determination

Whole blood samples were used for the determination of the heamatological indices using automated hematology auto machine -Mindray BC 5300 (UK).

Estimation of lipid profile

Serum cholesterol and high density lipoprotein were determined using the procedure of Allain et al. (1974). Total triglycerides were determined by the method of Jacobs and Denmark (1960). LDL was calculated by dividing triglycerides by 5.

Preparation of homogenate

Excised pancreas tissues were homogenized in phosphate buffer (0.1 M, pH 7.4), and centrifuged at 10,000 g for 10 min at 4 °C. The protein content was assayed using protocol of Bradford (1976).

Table 1 Effects of methanol extract of *Solanum macrocarpon* and its fractions on blood glucose concentration (mg/dL) of rats of diabetic rats

	0	7	14	21	28
Control	90.67 ± 12.42	89.50 ± 7.89	90.07 ± 8.06	89.00 ± 6.00	88.33 ± 6.88
DC	285.00 ± 16.37 ^a	385.85 ± 23.50 ^a	468.00 ± 49.92 ^a	454.00 ± 36.40 ^a	495.33 ± 24.74 ^a
SME	300.67 ± 10.69 ^a	270.30 ± 18.50 ^{ab}	250.07 ± 23.69 ^{ab}	203.33 ± 35.56 ^{ab}	179.00 ± 10.00 ^{ab}
ETA	279.33 ± 28.57 ^a	240.15 ± 15.50 ^{ab}	205.33 ± 16.50 ^{ab}	160.00 ± 10.00 ^{ab}	114.00 ± 8.18 ^{ab}
BUT	274.33 ± 15.01 ^a	256.62 ± 20.56 ^{ab}	190.33 ± 23.86 ^{ab}	145.22 ± 16.74 ^{ab}	139.33 ± 8.08 ^{ab}
GLIB	268.67 ± 8.02 ^a	201.15 ± 11.25 ^{ab}	137.67 ± 11.59 ^{ab}	120.00 ± 8.88 ^{ab}	105.33 ± 4.51 ^{ab}

Values are Mean ± SD (n=6)

^a p < 0.05 when control group were compared with experimental groups, ^b p < 0.05 when diabetic group were compared with treated groups

Table 2 Effects of methanol extract of *Solanum macrocarpon* and its fractions on Weight (g) of diabetic rats

	0	7	14	21	28
Control	140.56 ± 3.45	153.00 ± 6.25	168.67 ± 2.51	188.00 ± 8.71	203.33 ± 8.79
DC	142.70 ± 2.18	148.67 ± 6.11 ^a	151.00 ± 6.24 ^a	162.67 ± 3.51 ^a	165.67 ± 2.08 ^a
SME	145.15 ± 3.10	154.67 ± 2.30 ^a	162.67 ± 3.05 ^b	176.00 ± 3.00 ^{ab}	187.00 ± 5.00 ^{ab}
ETA	142.56 ± 2.88	158.00 ± 2.51 ^a	166.00 ± 3.60 ^b	180.00 ± 2.65 ^b	194.00 ± 3.01 ^{ab}
BUT	140.12 ± 3.10	153.67 ± 3.51 ^a	163.00 ± 3.00 ^b	172.67 ± 3.15 ^b	182.00 ± 7.94 ^{ab}
GLIB	139.80 ± 3.99	154.67 ± 7.57 ^a	163.67 ± 7.57 ^b	173.33 ± 5.51 ^b	190.67 ± 4.72 ^{ab}

Values are Mean ± SD (n=6)

^a p < 0.05 when control group were compared with experimental groups, ^b p < 0.05 when diabetic group were compared with treated groups

Markers of oxidative stress and antioxidant status determination

Lipid peroxidation was evaluated using the method of Farombi et al. (2000). Nitric oxide was assayed based on the method of (Green et al. 1982). Reduced glutathione (GSH) was measured using the procedure of (Jollow et al. 1974). Glutathione peroxidase (GPx) was measured by the protocol of (Rotruck et al. 1973). Superoxide dismutase (SOD) was evaluated by the procedure of (Misra and Fridovich 1972). Catalase (CAT) was measured using the method of (Clairborne 1995).

Histopathology

Pancreas were fixed in 10% formaldehyde for 24 h, and processed using the method of Avwioro (2010).

Statistical analysis

Data are presented as the mean ± SD. The significance of the differences between means was established by ANOVA, p < 0.05 using SPSS and charts were drawn with graph pad prism 9.

Results

As shown in Table 1, induction of DM led to elevation in blood glucose level of diabetic rats. However, treatment with the extract(s) lowered the level of FBG significantly

(p < 0.05) in the diabetic rats. Table 2 presents the effect of the treatment on the body weight of diabetic rats. There was reduction in the body weight of the diabetic rats when compared with the control rats. Administration of the extract(s) was able to increase the weight of diabetic rats significantly (p < 0.05) in relation to untreated diabetic rats. The impact of the extract(s) on metabolic output of diabetic rats is shown in Fig. 1. The increased food intake, water consumption and urine output were significantly (p < 0.05) reduced. Figure 2 presents the effect of treatment on OGTT. After 30 min of glucose load, diabetic rats treated with the extract(s) have started showing decline in their blood glucose levels unlike diabetic control rats. The role of treatment on hematological indices of the diabetic rats is shown in Table 3. Packed cell volume (PCV), platelets (PLT), red blood cell (RBC) and hemoglobin (Hg) levels were declined while white blood cell (WBC) was increased in diabetic rats. Treatment of diabetic rats with the vegetable extract(s) significantly normalized these parameters (p < 0.05) against the control rats. Figure 3 shows the effect of the treatment on the lipid profile; total cholesterol, triglycerides, and LDL-cholesterol were significantly increased while HDL-cholesterol was decreased in diabetic rats. Upon administration of the extract(s) for 28 days, the parameters were significantly (p < 0.05) reversed in diabetic rats. The effect of the treatment with extract(s) on lipid peroxidation (LPO), nitric oxide (NO) and H₂O₂ is shown in Fig. 4. The formation of lipid peroxide, nitric oxide and hydrogen peroxide were significantly (p < 0.05) increased in diabetic rats. Treatment with extract(s) was able to decrease the generation of these free radicals significantly (p < 0.05). The role of treatment

Fig. 1 Effects of methanol extract of *Solanum macrocarpon* and its fractions on metabolic output of diabetic rats. ^a $p < 0.05$ when control group were compared with experimental groups, ^b $p < 0.05$ when diabetic group were compared with treated groups

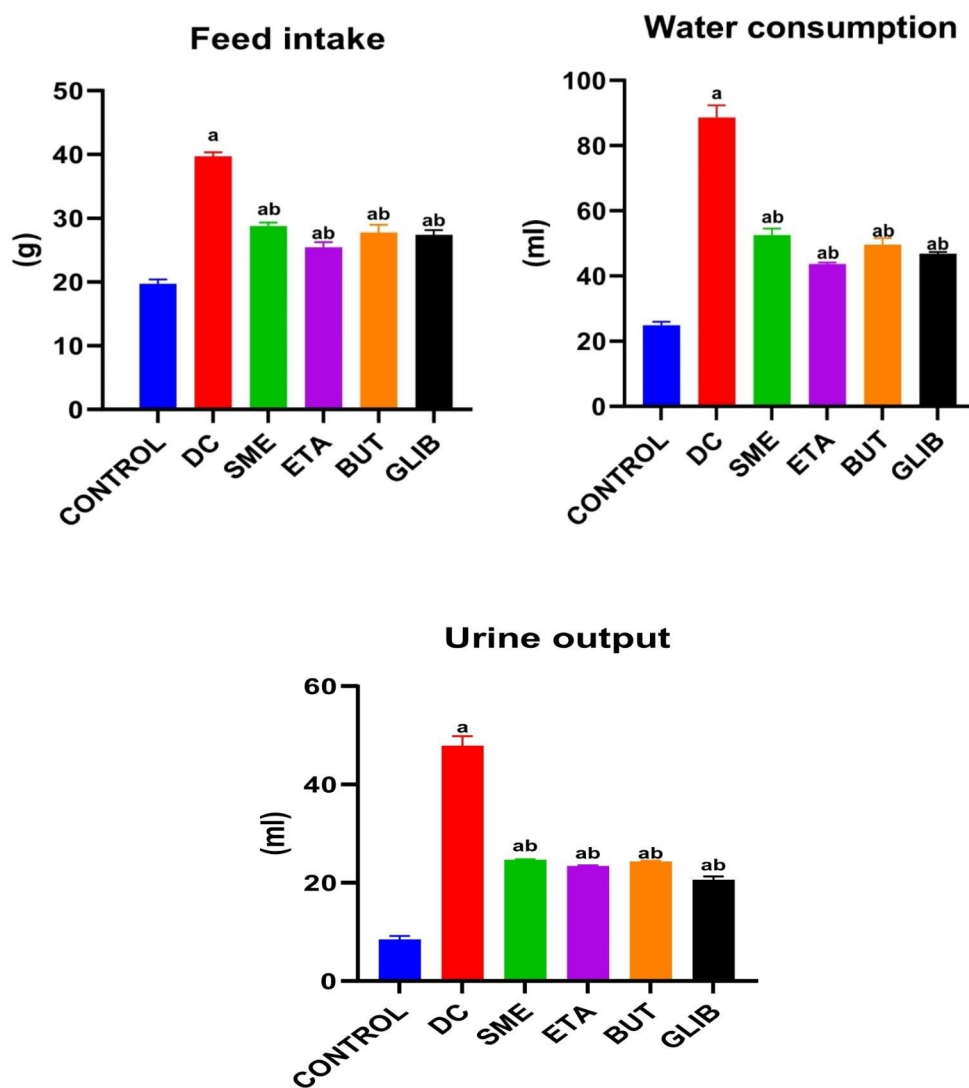


Fig. 2 Effects of methanol extract of *Solanum macrocarpon* and its fractions on OGTT of diabetic rats. ^a $p < 0.05$ when control group were compared with experimental groups, ^b $p < 0.05$ when diabetic group were compared with treated groups

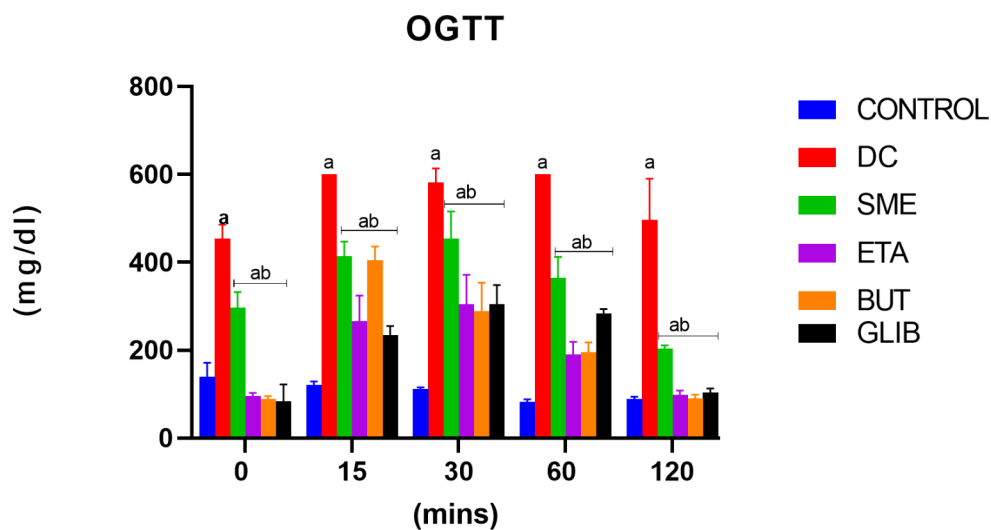
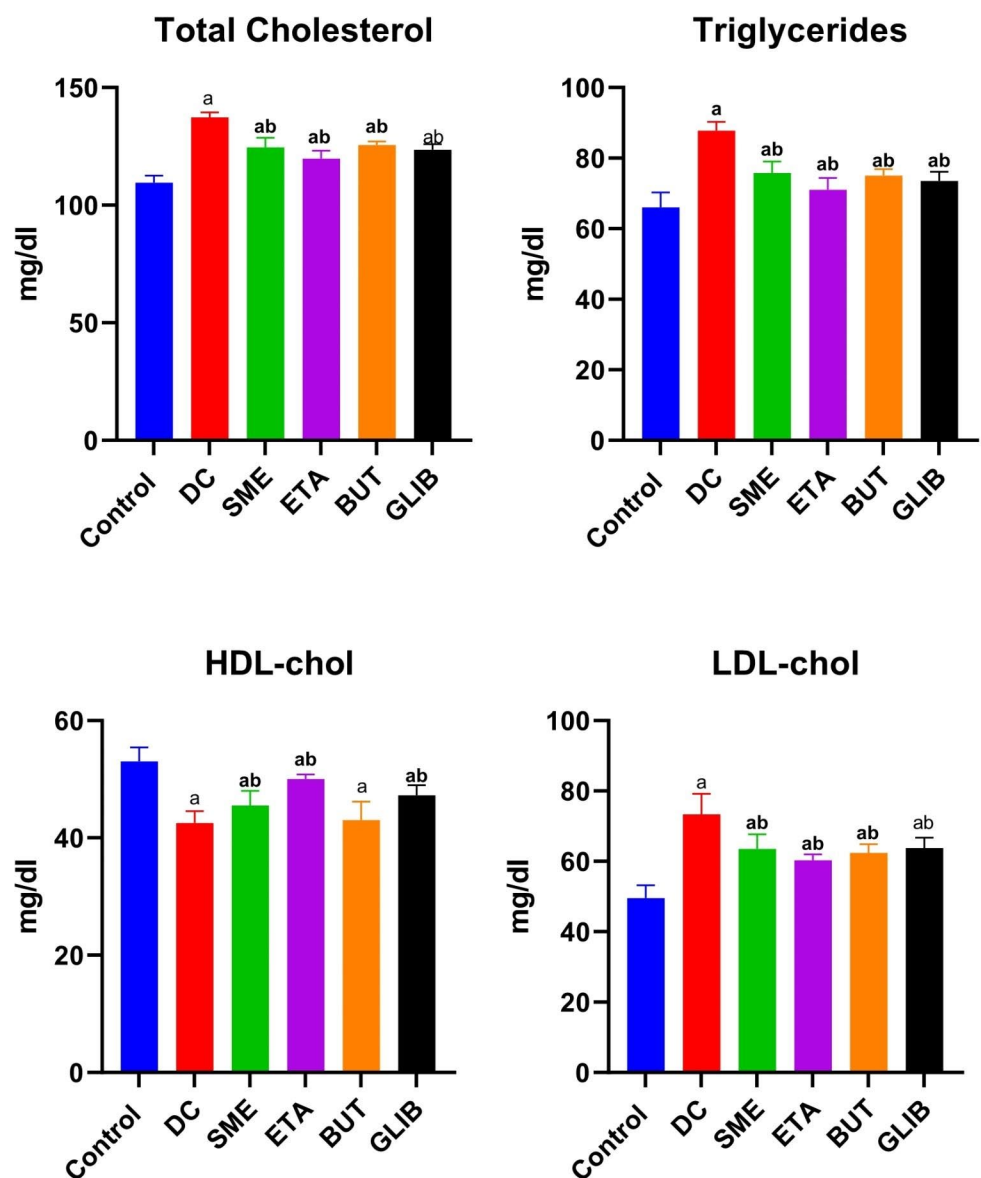


Table 3 Effects of methanol extract of *Solanum macrocarpon* and its fractions on hematological indices of diabetic rats

	Control	DC	SME	ETA	BUT	GLIB
PVC (%)	43.00 ± 1.02	34.33 ± 0.60 ^a	37.67 ± 0.58 ^{ab}	38.33 ± 0.58 ^{ab}	37.67 ± 0.53 ^{ab}	40.67 ± 1.15 ^{ab}
RBC (10 ⁶) cell/mm ³	12.02 ± 0.34	7.23 ± 0.27 ^a	7.65 ± 0.39 ^b	9.25 ± 0.96 ^{ab}	8.85 ± 0.22 ^{ab}	9.93 ± 0.06 ^{ab}
WBC (10 ³) cell/mm ³	6.68 ± 0.30	10.62 ± 0.57 ^a	8.10 ± 0.30 ^{ab}	8.08 ± 0.63 ^{ab}	7.29 ± 0.74 ^b	8.50 ± 0.35 ^{ab}
PLT (10 ⁵) Cell/mm ³	6.18 ± 0.85	2.96 ± 0.12 ^a	4.33 ± 0.44 ^{ab}	4.30 ± 0.92 ^{ab}	3.97 ± 0.42 ^{ab}	5.54 ± 1.25 ^{ab}
HB (g/L)	15.2 ± 0.89	9.93 ± 0.46 ^a	11.60 ± 0.70 ^{ab}	12.03 ± 0.25 ^{ab}	12.73 ± 0.47 ^{ab}	14.00 ± 0.10 ^{ab}
N (%)	63.33 ± 6.11	59.00 ± 7.00	66.67 ± 3.21	63.00 ± 1.00	63.33 ± 6.66	65.33 ± 7.51
L (%)	36.67 ± 6.10	40.67 ± 7.02 ^a	32.33 ± 3.21	36.33 ± 1.15	35.67 ± 6.65	34.67 ± 7.50
M (%)	00	00	0.67	0.33	0.67	00
E (%)	00	0.33	0.33	0.33	0.33	00
B (%)	00	00	00	00	00	00

^a p < 0.05 when control group were compared with experimental groups, ^b p < 0.05 when diabetic group were compared with treated groups

Fig. 3 Effects of methanol extract of *Solanum macrocarpon* and its fractions on Lipid profiles of diabetic rats. ^a p < 0.05 when control group were compared with experimental groups, ^b p < 0.05 when diabetic group were compared with treated groups



on GSH, GPX, GST, SOD and CAT is shown in Fig. 5. There was significant ($p < 0.05$) reduction in GSH level and activities of GPX, GST, SOD and CAT of diabetic rats which was significantly modulated by administration of the extract(s) for 28 days. The effect of the administration of the extract(s) on the structural integrity (Pancreas) of the diabetic rats is presented in Fig. 6. The control rats revealed normal architecture while the diabetic control rats showed poor architecture with severe fibrosis and diffused islet of Langerhans. The treated groups showed moderate architecture with mild infiltration of inflammatory cells.

Discussion

Numerous studies have reported positive results on the utilization of vegetable plants in the treatment of streptozotocin - induced diabetes and its associated ailments in experimental animals (Omoboyowa et al. 2020; Boye et al. 2020; Ajiboye et al. 2021). Apart from hyperglycemia,

the induction of DM is usually accompanied by enhanced food intake, weight loss, urination and thirst (Ibrahim et al. 2018). The positive responses on these metabolic parameters upon treatment might be attributed to the anti-hyperglycemic ability of the vegetable extract(s) which may be linked to their capacity to regenerate of pancreas β -cells (Karigidi and Olaiya 2020a). An OGTT is a more dependable index of untimely irregularity in glucose metabolism than fasting blood glucose (Jagannathan et al. 2020). The improvement in the OGTT of diabetic rats further confirms the antihyperglycemic potential of the extract(s). Enhanced blood glucose concentration promotes oxidative attachment of glucose to hemoglobin leading to its loss of structure and function (Dordevic et al. 2017). Anaemia in DM is due to the elevated non-enzymatic glycosylation of membrane proteins in RBC. Also, white blood cells are activated by advanced glycation products. In the present study, the vegetable extract(s) modulate the anaemia and abnormalities of immune functions. Induced DM lead to a persistent increase in cholesterol, triglycerides and decrease in HDL

Fig. 4 Effects of methanol extract of *Solanum macrocarpon* and its fractions on biomarkers of oxidative stress of diabetic rats. ^a $p < 0.05$ when control group were compared with experimental groups, ^b $p < 0.05$ when diabetic group were compared with treated groups

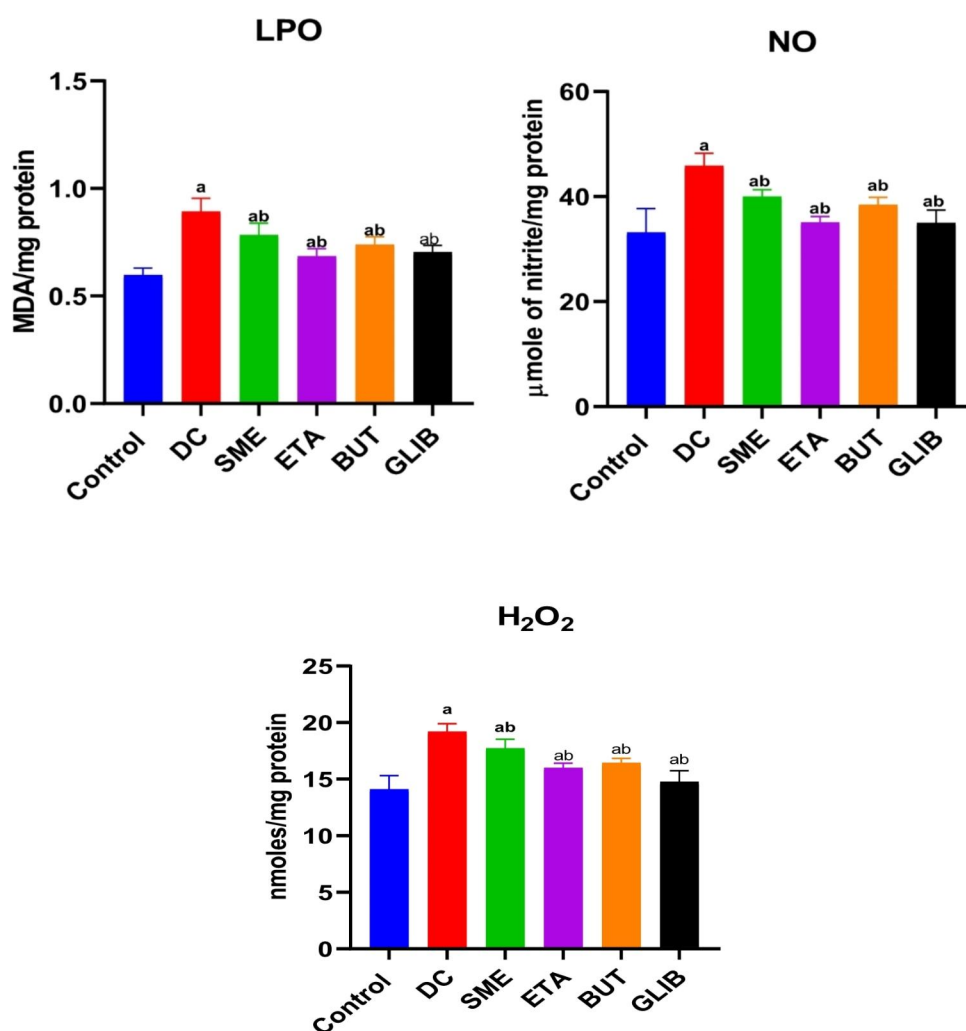
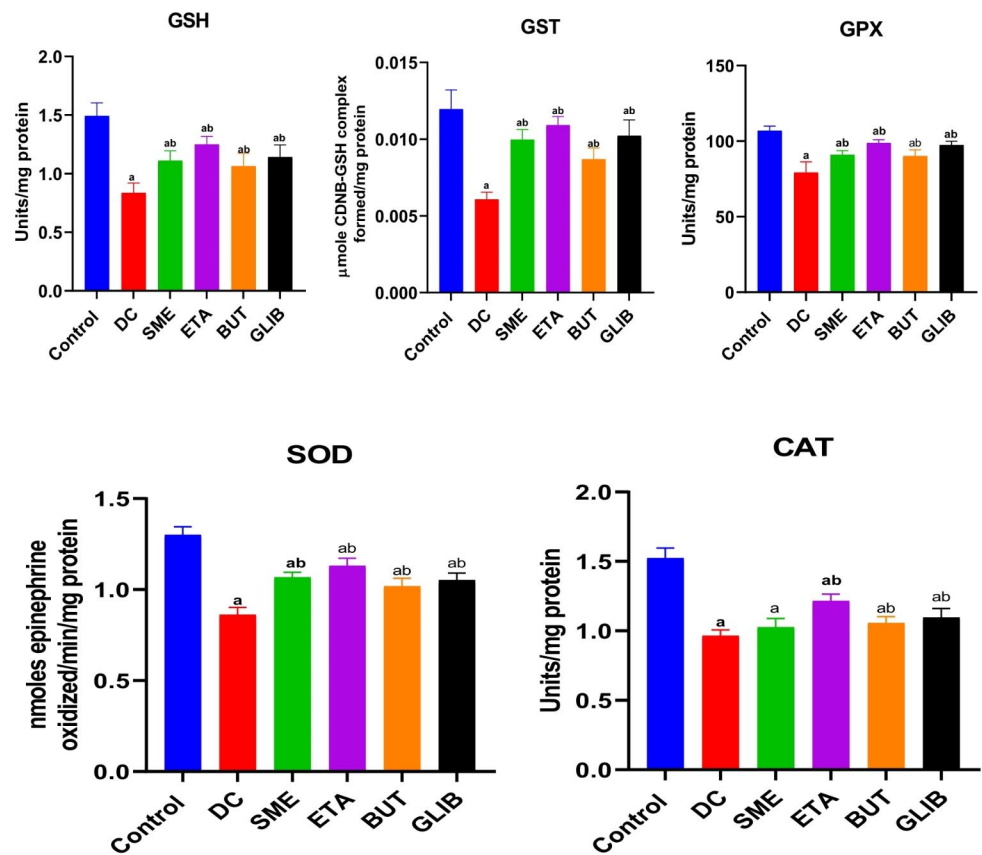


Fig. 5 Effects of methanol extract of *Solanum macrocarpon* and its fractions on GSH, GPx, GST, SOD and CAT. ^a $p < 0.05$ when control group were compared with experimental groups, ^b $p < 0.05$ when diabetic group were compared with treated groups



concentrations as reported by similar studies (Karigidi et al. 2020). In DM, hormone-sensitive lipase is activated leading to excessive liberation of free fatty acids (FFAs) from adipose tissue. Therefore, the marked hyperlipidemia that is usually associated with DM may be considered a result of the uncontrolled activities of lipolytic hormones on fat deposits (Cyriac and Eswaran 2016). In this study, these parameters were mitigated indicating that treatment with the vegetable can reduce the risk of cardiovascular diseases in DM.

These overproduced free radicals in DM attack biological membranes and different biomolecules leading to membrane damage and loss of functions of many organs. Treatment with the SM extract(s) was able to modulate the elevated free radical production. The reduced free radicals production might be attributed to the normalization of glucose homeostasis in treated diabetic rats. In response to increased ROS production, antioxidants are activated to mop up ROS in order to maintain REDOX homeostasis in the body (Abdulwahab et al. 2021). The enhanced antioxidant status of the treated diabetic rats might be attributed

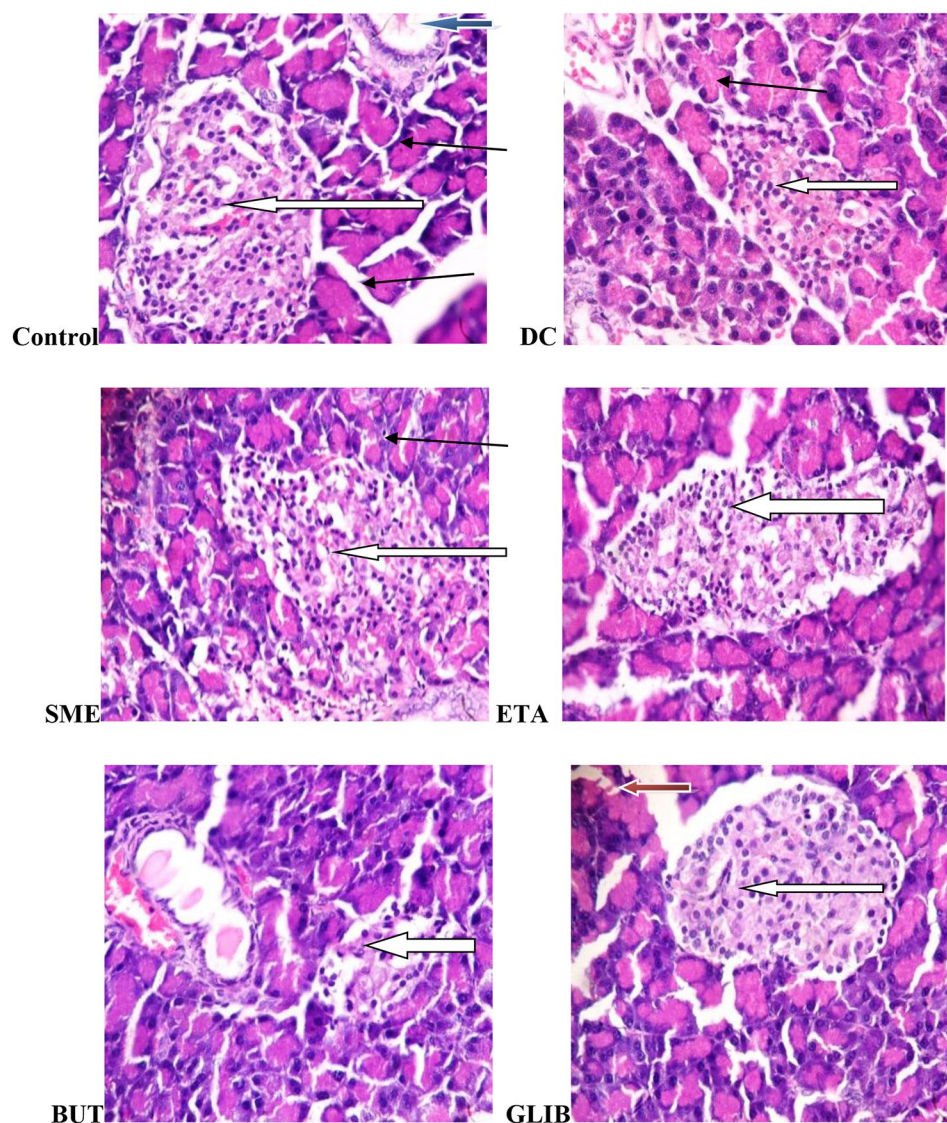
to presence of antioxidant molecules in SM (Idowu et al. 2021). Antidiabetic property of the SM was further confirmed on its ability to promote regeneration of pancreas' cell after induction of DM. In the present study, histopathology plates revealed improved structural integrity in pancreas of treated diabetic rats.

Conclusion

Data obtained in the present study have shown that *Solanum macrocarpon* can lower blood glucose level, improved glucose tolerance, modulate aberrant lipid and hematological indices and mitigate hyperglycemia - mediated oxidative stress in pancreas; thereby justifying the use of this vegetable for treatment of diabetes mellitus in folk medicine.

Authors' contribution OJA designed, performed experiment and wrote the first draft of manuscript, KOK performed experiment and statistical analysis of data, MOA performed experiment and statistical analysis of data COO designed, supervised and reviewed the final version of the manuscript.

Fig. 6 Effects of methanol extract of *Solanum macrocarpon* and its fractions on Histopathology of diabetic rats (×400)



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Declarations

Competing interests The authors have no competing interest to declare.

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