



Evaluation of Anti-Diabetic and Antioxidant Potential of *Vernonia auriculifera* Bark Extract in Streptozotocin-Induced Diabetic Wistar Rats

Lucky A. Mahmoud^{1*}, Naomi Bisem¹, Geoffrey Kiptoo², Stephen Barasa¹, Julius Koech¹

¹Department of Chemistry and Biochemistry, University of Eldoret, Eldoret, Kenya

²Department of Biochemistry and Clinical Chemistry, School of Medicine, Moi University, Kesses, Kenya

Email: *luckyabdirizak@gmail.com

How to cite this paper: Mahmoud, L.A., Bisem, N., Kiptoo, G., Barasa, S. and Koech, J. (2026) Evaluation of Anti-Diabetic and Antioxidant Potential of *Vernonia auriculifera* Bark Extract in Streptozotocin-Induced Diabetic Wistar Rats. *Open Access Library Journal*, 13: e15557.

<https://doi.org/10.4236/oalib.1115557>

Received: May 29, 2026

Accepted: July 3, 2026

Published: July 6, 2026

Copyright © 2026 by author(s) and Open Access Library Inc.

This work is licensed under the Creative Commons Attribution International License (CC BY 4.0).

<http://creativecommons.org/licenses/by/4.0/>



Open Access

Abstract

Background: Diabetes mellitus is a condition characterised by elevated blood glucose levels and oxidative stress, leading to various complications. Medicinal plants represent an important but under utilised source of antidiabetic and antioxidant phytochemical compounds. **Objective:** This study evaluated the phytochemical composition, *in vitro* antioxidant activities, and *in vivo* antidiabetic potential of *Vernonia auriculifera* Hiern bark extract in streptozotocin-induced diabetic Wistar rats. **Methods:** The methanolic, ethanolic, and aqueous extracts of the bark were subjected to phytochemical screening. Antioxidant properties were evaluated *in vitro* by measuring the ferric reducing power (FRAP) and scavenging effect against hydrogen peroxide (H₂O₂). Twenty-five male albino Wistar rats were randomly assigned to five groups: normal control, diabetic control, diabetic treated with 200 mg/kg extract, diabetic treated with 400 mg/kg extract, and diabetic treated with 100 mg/kg metformin. Extracts and metformin were orally administered for 21 days. **Results:** Phytochemical screening revealed the presence of flavonoids, alkaloids, tannins, glycosides, terpenoids, saponins, and anthraquinones in the methanol extract. The methanol extract showed maximum antioxidant potential, with H₂O₂ scavenging activity at 60 µg/mL (85%), comparable to ascorbic acid. *In vivo*, the 400 mg/kg dose significantly reduced blood glucose in diabetic animals from 280 to 97 mg/dL ($P < 0.01$), outperforming metformin (111 mg/dL). Treatment also significantly decreased malondialdehyde (MDA) concentrations and improved the lipid profile. The 200 mg/kg dose produced greater reductions in liver enzyme activities (GGT, ALT, ALP). However, elevated AST at 400 mg/kg, higher triglycerides at 200 mg/kg, and elevated urea at 400 mg/kg indicate dose-dependent safety concerns that require further investigation. **Conclusion:** *Vernonia auriculifera* bark extract, particularly at 400 mg/kg, demonstrates significant

antidiabetic and antioxidant activities in streptozotocin-induced diabetic Wistar rats.

Subject Areas

Biological Chemistry

Keywords

Antidiabetic Activity, Antioxidant, Phytochemicals, Streptozotocin, *Vernonia auriculifera*, Wistar Rats, Oxidative Stress, Dyslipidaemia

1. Introduction

Diabetes mellitus (DM) is a metabolic condition marked by hyperglycaemia arising from impaired insulin production and/or insulin resistance [1]. According to the International Diabetes Federation (IDF), more than 537 million individuals worldwide were living with diabetes in 2021, with projections exceeding 780 million by 2045, posing a significant socio-economic burden on healthcare facilities, particularly in developing countries [2].

Type 2 diabetes mellitus (T2DM) accounts for 90% - 95% of all DM cases and is characterised by insulin resistance in peripheral tissues and pancreatic β -cell dysfunction [3]. Persistent hyperglycaemia promotes the overproduction of reactive oxygen species (ROS), leading to oxidative stress, β -cell destruction, inflammation, and complications such as diabetic nephropathy, retinopathy, neuropathy, and cardiovascular disease [4] [5].

Although conventional drugs such as metformin, thiazolidinediones, and sulphonylureas aid in glucose regulation, their adverse effects and costs have spurred interest in natural antidiabetic agents with multi-faceted mechanisms, lower toxicity, and greater affordability in developing countries [6].

The Asteraceae plant *Vernonia auriculifera* Hiern is an indigenous medicinal plant of sub-Saharan Africa used traditionally in the management of hyperglycaemia and metabolic disorders. Despite its ethnopharmacological relevance, its scientific characterisation for antidiabetic and antioxidant properties remains inadequate. Previous studies on the sister species *V. amygdalina* have demonstrated considerable antidiabetic, antioxidant, and hypolipidaemic potential [7]-[9]. The present study was therefore designed to: 1) determine the phytochemical constituents of methanolic, ethanolic, and aqueous bark extracts of *V. auriculifera*; 2) evaluate the antioxidant potential of the extracts *in vitro*; and 3) assess the antidiabetic activity of the plant in streptozotocin (STZ)-induced diabetic Wistar rats *in vivo*. It should be noted that the STZ-only induction protocol predominantly reflects insulin-deficient (type 1-like) diabetes; findings from this model should therefore be interpreted with caution and not directly extrapolated to type 2 diabetes mellitus without further validation using complementary models such as

high-fat diet/STZ combination protocols.

2. Materials and Methods

2.1. Ethical Approval

All animal experiments were performed in adherence to international guidelines on animal experimentation and were ethically approved by the Institutional Animal Use and Care Committee at the University of Eastern Africa, Baraton. All animals were treated humanely throughout the experiment and had unrestricted access to standard rodent pellets and water.

2.2. Plant Material and Extraction

The bark of *Vernonia auriculifera* was harvested from Eldoret, Uasin Gishu County, Kenya (0.5206°N, 35.2698°E). authenticated by a botanist at the University of Eldoret, and a voucher specimen deposited in the University of Eldoret Herbarium, voucher number; UOE/BR/2025/15. The bark was air-dried away from direct sunlight. The dried plant material was ground into a fine powder. Sequential cold maceration was performed for 72 hours at a bark-to-solvent ratio of 1:10 (w/v) for each solvent (methanol, ethanol, and distilled water). The extracts were filtered, evaporated to dryness under reduced pressure using a rotary evaporator, and the percentage extraction yields calculated (methanol 18.4%; ethanol:14.7%; aqueous: 10.2%). The dried extracts were stored at 4°C until further use. For *in vivo* dosing, extracts were dissolved in distilled water and administered orally by gavage at a volume of 10 mL/kg body weight.

2.3. Phytochemical Screening

Qualitative phytochemical analyses for secondary metabolites—including flavonoids, alkaloids, tannins, glycosides, terpenoids, steroids, saponins, and anthraquinones—were performed on all three extracts using established conventional methods [10] [11].

2.4. *In Vitro* Antioxidant Activities

The ferric reducing antioxidant power (FRAP) assay was evaluated spectrophotometrically at 700 nm across five concentrations (100 - 500 µg/mL), with ascorbic acid as the reference standard. Hydrogen peroxide (H₂O₂) scavenging activity was determined at 230 nm at three concentrations (20, 40, and 62.5 µg/mL).

2.5. Experimental Animals and Diabetes Induction

Twenty-five male Wistar rats (body weight 180 - 220 g) were randomly assigned to five groups of five animals each using simple randomization (random number table): Group I—Normal Control (NC); Group II—Diabetic Control (DC); Group III—Diabetic + 200 mg/kg body weight methanol extract (DL); Group IV—Diabetic + 400 mg/kg body weight methanol extract (DH); and Group V—Diabetic + 100 mg/kg body weight metformin (MET). Diabetes was induced by a single in-

traperitoneal injection of STZ (60 mg/kg body weight) dissolved in 0.1 M citrate buffer (pH 4.5). Seventy-two hours after STZ injection, tail-vein blood glucose was measured following an overnight fast (12 hours); rats with fasting blood glucose ≥ 200 mg/dL were confirmed diabetic and included in the study. All 25 rats completed the study; no animals were excluded after induction. Treatment began on Day 0 (the day after diabetes confirmation) and continued for 21 days (Weeks 1 - 3 corresponding to Days 1 - 7, 8 - 14, and 15 - 21 respectively; Week 4 measurements were taken at Day 21). The sample size of five per group was based on prior similar studies and was consistent with ethical minimisation guidelines; a formal power analysis was not performed.

2.6. Biochemical Analyses

Blood glucose concentrations were measured weekly using a glucometer. Body weights were recorded on Days 0, 7, 14, and 21. On Day 22 (the day following treatment completion), all animals were euthanised by lethal anaesthetic injection and blood samples were collected by cardiac puncture. Serum was separated by centrifugation and used for the determination of lipid profile (total cholesterol, triglycerides, HDL-C, LDL-C), liver function tests (GGT, AST, ALT, ALP, total protein, albumin, bilirubin), and kidney function tests (urea, creatinine) using standard enzymatic colorimetric reagents. Hepatic tissue malondialdehyde (MDA) content, an index of lipid peroxidation, was determined using the thiobarbituric acid reactive substances (TBARS) assay [12].

2.7. Statistical Analysis

Data are expressed as mean $\pm$ standard error of the mean (SEM). Statistical comparisons were made using one-way ANOVA followed by Tukey's post hoc test. A p-value of <0.05 was considered statistically significant. Analyses were performed using Microsoft Excel and R software. One-way ANOVA was applied independently at each time point for the weekly glucose and body weight data; while a repeated-measures ANOVA would be more appropriate for within-subject longitudinal comparisons, the one-way approach was used here due to the exploratory nature of the study. Future studies should employ repeated-measures ANOVA or mixed-effects models to better account for the correlated structure of repeated observations from the same animals.

3. Results

3.1. Phytochemical Composition

Qualitative phytochemical analysis revealed that the methanol extract contained the greatest diversity of secondary metabolites—flavonoids, alkaloids, tannins, glycosides, terpenoids, anthraquinones, and saponins—but lacked steroids. The aqueous extract was devoid of glycosides and terpenoids but contained steroids. The ethanol extract profile closely resembled that of the methanol extract, also lacking steroids (Table 1).

Table 1. Phytochemical composition of *Vernonia auriculifera* bark extracts.

Phytochemical	Methanol Extract	Aqueous Extract	Ethanol Extract
Flavonoids	+	+	+
Alkaloids	+	+	+
Tannins	+	+	+
Glycosides	+	–	+
Terpenoids	+	–	+
Steroids	–	+	–
Anthraquinones	+	+	+
Saponins	+	+	+

+: Present; –: Absent.

3.2. *In Vitro* Antioxidant Activity

3.2.1. Ferric Reducing Power

All three extracts demonstrated dose-dependent ferric reducing activity across concentrations of 100 - 500 µg/mL (**Table 2**). The methanol extract exhibited reducing capacity (OD = 1.716 - 1.764) closely comparable to ascorbic acid (OD = 1.727 - 1.805), followed by the ethanol extract (OD = 1.660 - 1.752).

Table 2. Ferric reducing power (Absorbance at 700 nm) of *V. auriculifera* bark extracts.

Conc. (µg/mL)	Methanol Extract	Ascorbic Acid	Ethanol Extract	Aqueous Extract
100	1.724	1.734	1.717	1.708
200	1.748	1.805	1.702	1.671
300	1.716	1.727	1.676	1.169
400	1.764	1.799	1.752	1.663
500	1.719	1.751	1.720	1.660

Values represent mean absorbance at 700 nm.

3.2.2. Hydrogen Peroxide Scavenging Activity

All extracts demonstrated concentration-dependent H₂O₂ scavenging activity (**Figure 1**). At 20 µg/mL, the methanol extract scavenged 60% and the aqueous extract scavenged 45% of H₂O₂, compared to 85% for ascorbic acid. At 40 µg/mL, these values increased to 75%, 60%, and 90%, respectively (P < 0.05), confirming significant antioxidant efficacy.

3.3. Blood Glucose Levels

All diabetic groups exhibited baseline blood glucose concentrations between 277 - 283 mg/dL following STZ induction, confirming successful diabetes induction. Treatment with the 400 mg/kg extract produced the greatest hypoglycaemic effect, reducing blood glucose from 280 ± 10 mg/dL at baseline to 97 ± 7 mg/dL at Week

4 ($P < 0.01$), which was lower than that achieved with metformin (111 ± 9 mg/dL) (Table 3).

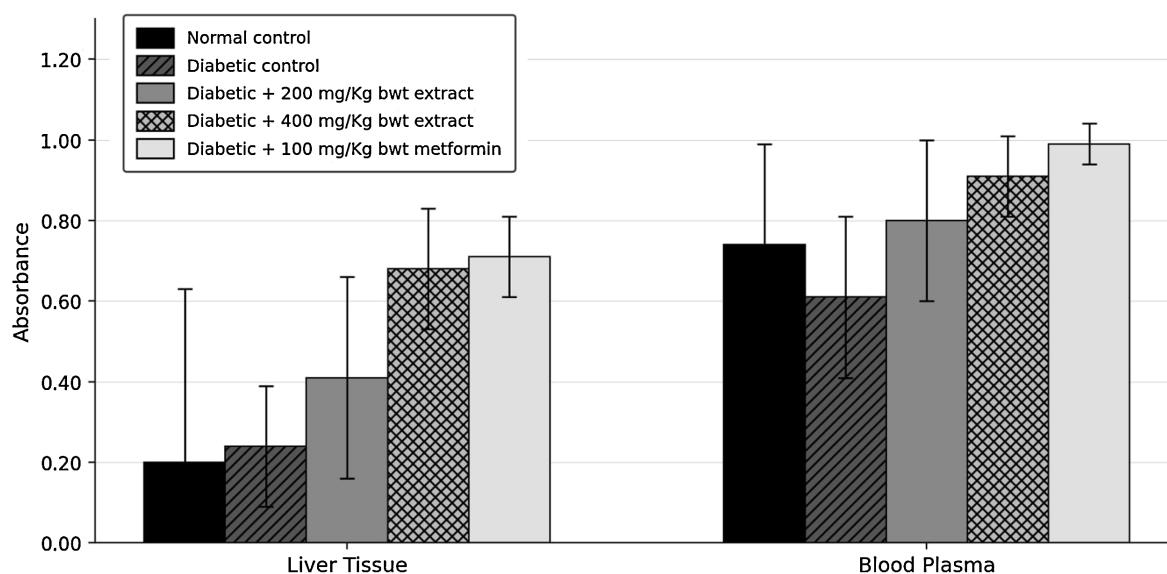


Figure 1. Hydrogen peroxide scavenging activity (%) of methanol, aqueous bark extracts of *V. auriculifera*, and ascorbic acid at different concentrations.

Table 3. Blood glucose levels (mg/dL) across treatment groups.

Group	Day 0	Week 1	Week 2	Week 3	Week 4
Diabetic Control	283 ± 9	274 ± 11	272 ± 12	266 ± 17	264 ± 8
Low-dose (200 mg/kg)	277 ± 10	240 ± 10	200 ± 11	187 ± 8	167 ± 6
High-dose (400 mg/kg)	280 ± 10	215 ± 16	165 ± 10	125 ± 11	97 ± 7*
Metformin (100 mg/kg)	282 ± 14	214 ± 15	167 ± 11	132 ± 7	111 ± 9
Normal Control	90 ± 5	91 ± 4	88 ± 4	92 ± 5	90 ± 4

* $P < 0.01$ vs. Diabetic Control. Values expressed as mean ± SEM.

3.4. Body Weight Changes

The normal control group showed progressive weight gain (+9%) over the experimental period. All diabetic groups experienced weight loss relative to Day 0: the diabetic control (−13%), the 200 mg/kg extract group (−13%), and the 400 mg/kg extract group (−15%). The metformin-treated group showed the most favourable weight outcome among the diabetic groups (−9%) (Table 4).

3.5. Effects on Liver Tissue and Blood Plasma Ferric Reducing Capacity

In liver tissues, the normal control group exhibited the lowest absorbance (approximately 0.20), whereas diabetic control showed a slight increase (~0.23). Administration of the 200 mg/kg extract raised absorbance to ~0.41, and the 400 mg/kg extract to ~0.69. The metformin group recorded the highest liver tissue

absorbance (~ 0.72). Plasma absorbance values were consistently higher than liver tissue values across all groups. The normal control plasma absorbance was approximately 0.75, which declined in the diabetic control (~ 0.61). The 200 mg/kg extract restored plasma absorbance to ~ 0.79 , the 400 mg/kg extract to ~ 0.91 , and metformin yielded the highest value (~ 1.00) (**Figure 2**).

Table 4. Effects of *Vernonia auriculifera* bark extract on fasting body weight (FBW) of streptozotocin-induced diabetic rats over 21 days.

Treatment Group	Day 0 FBW (g)	Day 7 FBW (g)	Day 14 FBW (g)	Day 21 FBW (g)	% Change in Body Weight on 21 st Day
Normal control	155.73 $\pm$ 4.16	149.9 $\pm$ 2.71	157.78 $\pm$ 3.12	170.27 $\pm$ 5.08	+9
Diabetic control	146.42 $\pm$ 2.2	136.83 $\pm$ 2.04	127.42 $\pm$ 3.74	127.73 $\pm$ 3.8a	-13
Diabetic + 200 mg/kg bwt extract	151.2 $\pm$ 7.95	163.95 $\pm$ 6.74	150.56 $\pm$ 7.09	131.11 $\pm$ 4.47a	-13
Diabetic + 400 mg/kg bwt extract	151.32 $\pm$ 3.87	128.48 $\pm$ 6.69	141.06 $\pm$ 7.19	129.16 $\pm$ 6.4a	-15
Diabetic + 100 mg/kg bwt metformin	145.58 $\pm$ 3.36a	136.06 $\pm$ 1.78a	139.6 $\pm$ 4.22a	132.12 $\pm$ 1.84a	-9

Values expressed as mean $\pm$ SEM; a = significantly different from normal control ($P < 0.05$).

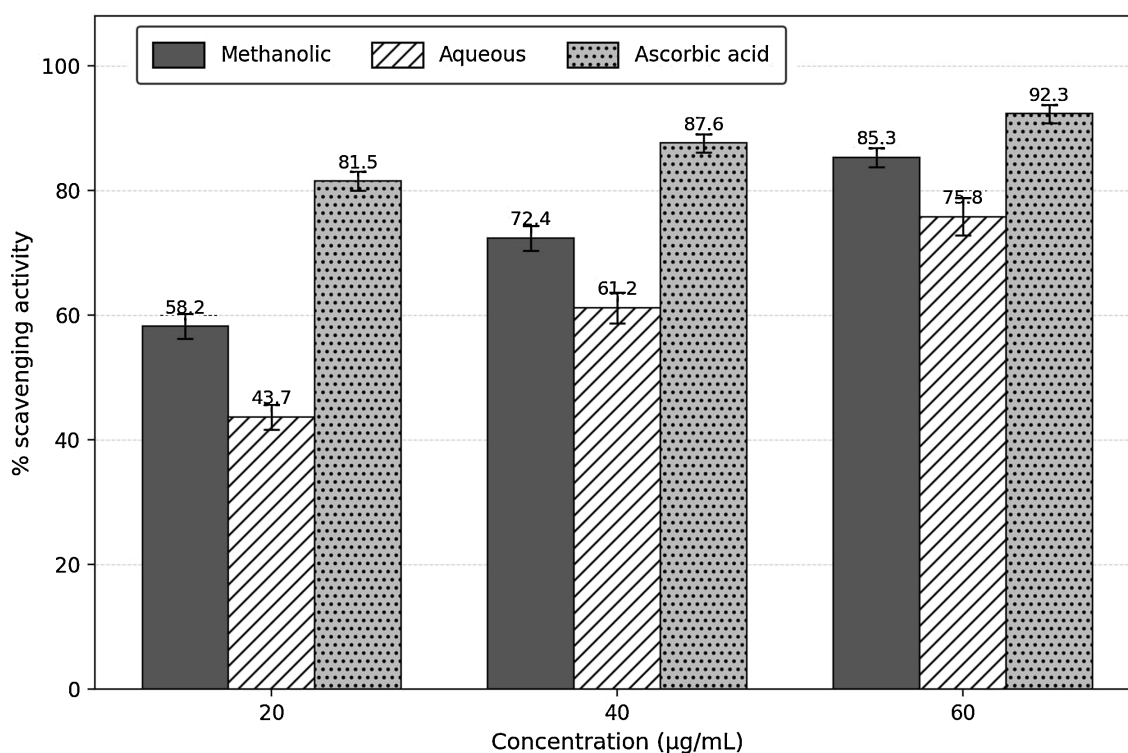


Figure 2. Absorbance of liver tissue and blood plasma ferric-reducing capacity across treatment groups in streptozotocin-induced diabetic Wistar rats treated with *V. auriculifera* bark extract and metformin.

3.6. Liver and Kidney Function Markers

Diabetes induction significantly elevated liver enzyme activities. Treatment with the 200 mg/kg extract produced the greatest reduction in GGT (3.85 ± 0.51 u/L vs. 11.38 ± 0.8 u/L in diabetic control), ALT (107.47 ± 5.58 u/L), and ALP (192.03

± 14.85 u/L). Albumin levels were most improved in the 200 mg/kg extract group (35.54 ± 1.83 g/L vs. 27.81 ± 1.1 g/L in diabetic control). Serum urea was significantly reduced in the 200 mg/kg extract group and the metformin group; however, urea levels were paradoxically elevated in the 400 mg/kg extract group (**Table 5**).

3.7. Serum Lipid Profile

Diabetes induction elevated triglycerides (1.37 vs. 0.93 mmol/L in normal control) and LDL-C (0.32 vs. 0.20 mmol/L), and reduced HDL-C (0.61 vs. 0.77 mmol/L). The 400 mg/kg extract normalised triglycerides (1.07 mmol/L) and HDL-C (0.75 mmol/L, approaching normal control values), and reduced LDL-C (0.24 mmol/L). The 200 mg/kg extract unexpectedly elevated triglycerides and total cholesterol (**Table 6**).

Table 5. Liver and kidney function biomarkers across treatment groups.

Parameter	Normal Control	Diabetic Control	DL 200 mg/kg	DH 400 mg/kg	Metformin
GGT (u/L)	2.61 ± 1.2	11.38 ± 0.8	3.85 ± 0.51	6.75 ± 0.42	5.71 ± 0.51
ALT (u/L)	66.43 ± 2.75	191.32 ± 16.39	107.47 ± 5.58	156.74 ± 4.45	137.31 ± 5.67
ALP (u/L)	97.35 ± 6.01	389.77 ± 11.35	192.03 ± 14.85	268.64 ± 7.43	295.03 ± 7.5
AST (u/L)	172.21 ± 9.08	267.85 ± 15.81	252.87 ± 5.14	322.14 ± 14.19	239.85 ± 9.04
Total Protein (g/L)	73.54 ± 2.83	58.56 ± 6.62	63.33 ± 3.84	62.5 ± 2.65	59.77 ± 3.64
Albumin (g/L)	42.9 ± 1.47	27.81 ± 1.1	35.54 ± 1.83	33.52 ± 0.71	34.26 ± 2.97
Urea (mmol/L)	8.11 ± 0.5	24.32 ± 2.15	18.32 ± 0.49	23.75 ± 1.03	18.65 ± 1.34
Creatinine (mmol/L)	31.9 ± 1.57	21.37 ± 2.73	21.54 ± 1.3	19.1 ± 0.72	22.75 ± 1.04

DL: Low-dose extract; DH: High-dose extract. Values expressed as mean $\pm$ SEM.

Table 6. Serum lipid profile across treatment groups.

Parameter (mmol/L)	Normal Control	Diabetic Control	DL 200 mg/kg	DH 400 mg/kg	Metformin
Triglycerides	0.93 ± 0.11	1.37 ± 0.16	$2.11 \pm 0.21^*$	1.07 ± 0.12	1.09 ± 0.11
Total Cholesterol	1.39 ± 0.12	1.37 ± 0.1	$1.55 \pm 0.15^*$	1.26 ± 0.1	1.23 ± 0.09
HDL-Cholesterol	0.77 ± 0.08	0.61 ± 0.08	0.60 ± 0.06	$0.75 \pm 0.07^\dagger$	0.68 ± 0.07
LDL-Cholesterol	0.20 ± 0.03	0.32 ± 0.04	0.30 ± 0.03	0.24 ± 0.03	0.22 ± 0.02

*P < 0.05 vs. Diabetic Control; † P < 0.05 vs. Diabetic Control. DL: Low-dose; DH: High-dose. Values expressed as mean $\pm$ SEM.

3.8. Lipid Peroxidation (MDA Levels)

Diabetic control rats exhibited the highest hepatic MDA levels (~ 2.95 μ M), reflecting severe oxidative stress. Treatment with the 400 mg/kg extract reduced MDA to ~ 1.53 μ M, slightly below the normal control (~ 1.65 μ M) and metformin-treated values (~ 1.68 μ M), indicating superior *in vivo* antioxidant activity at this dose (**Figure 3**).

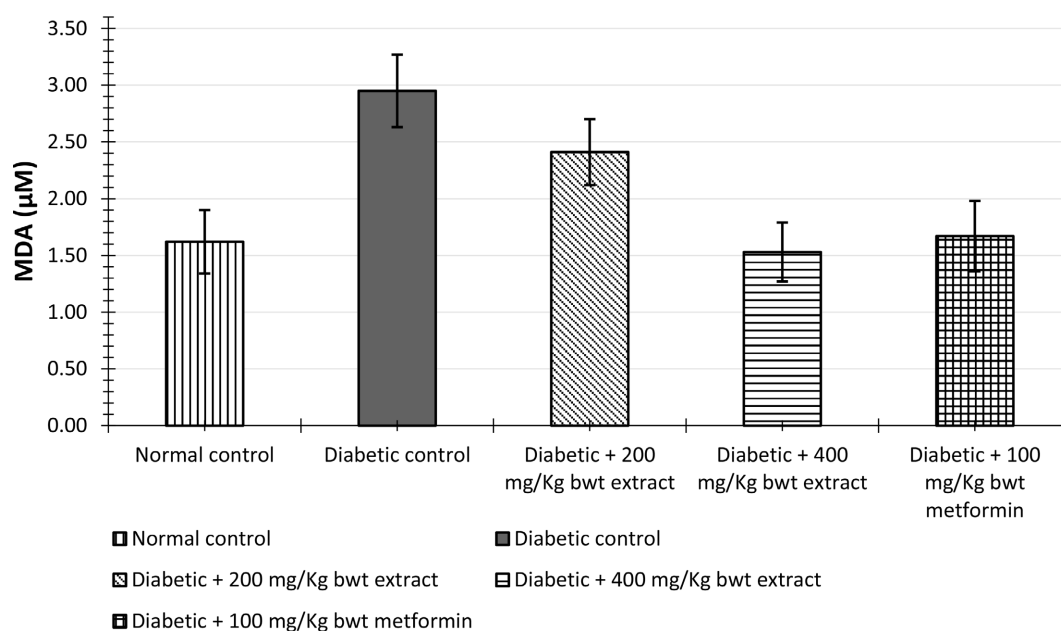


Figure 3. Effects of *Vernonia auriculifera* bark extract on lipid peroxidation (MDA levels) in liver tissues of streptozotocin-induced diabetic Wistar rats.

4. Discussion

This study provides a comprehensive pharmacological evaluation of *V. auriculifera* bark extract, characterising its phytochemical profile, antioxidant capacity, and antidiabetic efficacy in an STZ-induced rodent model.

The presence of flavonoids, tannins, saponins, alkaloids, and terpenoids in both methanol and ethanol extracts supports their established roles in glucose metabolism regulation. Flavonoids have been reported to inhibit α -amylase and α -glucosidase enzymes, reduce postprandial hyperglycaemia, and stimulate insulin secretion [13] [14]. Tannins retard intestinal glucose absorption, while saponins and alkaloids enhance insulin sensitivity [15]. The abundance of these active constituents in the methanol extract is consistent with the greater polarity of methanol in extracting polyphenols, as confirmed by Erasto *et al.* (2007) [7] in *V. amygdalina*.

The near-equivalent H_2O_2 scavenging activity between the methanol extract and ascorbic acid at 60 μ g/mL underscores the strong antioxidant capacity of the former, attributable to the electron-donating ability of polyphenolic constituents [16]. This mechanism is therapeutically relevant, since ROS-induced oxidative stress is implicated in pancreatic β -cell dysfunction and insulin resistance [4].

A notable observation in this study is the superior antihyperglycaemic effect of the 400 mg/kg dose (97 mg/dL at Week 4) over metformin (111 mg/dL). This may reflect the synergistic actions of flavonoids, saponins, and alkaloids in modulating glucose homeostasis through inhibition of hepatic gluconeogenesis, increased peripheral glucose uptake, and stimulation of insulin secretion—mechanisms analogous to those of metformin [17] [18]. Comparable dose-dependent antihyperglycaemic effects have been documented for *V. amygdalina* extract in STZ-in-

duced diabetic rats [8] [9]. The reduction of MDA by the 400 mg/kg extract to near-normal levels ($\sim 1.53 \mu\text{M}$ vs. $\sim 1.65 \mu\text{M}$ in normal control), slightly exceeding the effect of metformin ($\sim 1.68 \mu\text{M}$), provides compelling evidence of dose-dependent *in vivo* antioxidant activity, likely mediated through pathways similar to metformin's established inhibition of mitochondrial ROS production via AMPK activation [19]. This finding is consistent with reports by Maritim *et al.* (2003) and Patel *et al.* (2012) demonstrating that polyphenol-enriched plant extracts effectively reduce MDA in experimental diabetic models [20] [18].

The hepatoprotective activity of the 200 mg/kg extract, evidenced by significant reductions in GGT, ALT, and ALP, is likely attributable to antioxidant protection of hepatocytes from oxidative damage. However, the paradoxical elevation of AST at 400 mg/kg ($322.14 \pm 14.19 \text{ u/L}$ vs. $267.85 \pm 15.81 \text{ u/L}$ in diabetic control) raises a direct safety concern: while GGT, ALT, and ALP were reduced at this higher dose, the increase in AST suggests selective mitochondrial or membrane-associated hepatocellular stress that is not captured by the other liver enzymes alone. This dose-dependent divergence in liver enzyme responses likely reflects a ceiling effect beyond which extract constituents at higher concentrations may exert pro-oxidant or cytotoxic activity, as noted with polyphenol-rich extracts [21]. The elevated triglycerides at 200 mg/kg ($2.11 \pm 0.21 \text{ mmol/L}$) compared with both diabetic control (1.37 mmol/L) and normal control (0.93 mmol/L) is unexplained by the current data and may reflect dose-specific disruption of lipid metabolism, possibly via interference with lipoprotein lipase activity or fatty acid synthesis at that concentration; this warrants dedicated lipid metabolism investigation. Regarding renal markers, the higher serum urea at 400 mg/kg ($23.75 \pm 1.03 \text{ mmol/L}$, similar to diabetic control at $24.32 \pm 2.15 \text{ mmol/L}$) indicates absence of renal benefit at that dose, despite the apparent glucose lowering, and directly contradicts claims of kidney protection for the high dose. Notably, creatinine was lower in diabetic animals ($21.37 \pm 2.73 \text{ mmol/L}$) than in normal controls ($31.9 \pm 1.57 \text{ mmol/L}$) — a finding that may reflect reduced muscle mass in diabetic rats (cachexia) rather than improved renal filtration, and should not be interpreted as a kidney-protective effect without GFR confirmation.

Neither extract dose significantly ameliorated body weight loss in diabetic rats over 21 days, in contrast to metformin's more favourable weight retention (-9%). The modest weight effects of the extracts may be secondarily linked to their glucose-lowering and antioxidant protective actions rather than direct anabolic activity.

In terms of lipid profile, the 400 mg/kg dose demonstrated broad anti-hyperlipidaemic action—reducing LDL-C, normalising triglycerides, and restoring HDL-C toward normal values—comparable to metformin. The probable mechanism may involve inhibition of lipogenesis and HMG-CoA reductase activity by bioactive phytoconstituents.

5. Conclusion

Vernonia auriculifera bark extracts demonstrate substantial phytochemical diver-

sity, strong *in vitro* antioxidant potential, and significant antihyperglycaemic efficacy in an STZ-induced insulin-deficient rat model. The 400 mg/kg dose reduced fasting blood glucose significantly more than metformin at Week 4; however, this comparison is based on endpoint measurements only and should be interpreted cautiously given the exploratory study design and small group sizes. Hepatoprotective effects were more evident at 200 mg/kg, with better reductions in GGT, ALT, and ALP than at 400 mg/kg. Claims of superiority over metformin and kidney protection are not uniformly supported by the data: AST was elevated at 400 mg/kg, triglycerides were paradoxically elevated at 200 mg/kg, and urea at 400 mg/kg was not significantly different from the diabetic control, indicating an absence of renal benefit at that dose. These safety signals necessitate further investigation, including dose-response toxicity studies, repeated-measures statistical analysis, and validation in a type 2 diabetes model before broader conclusions can be drawn.

Acknowledgements

The authors thank the Department of Chemistry and Biochemistry, University of Eldoret, for laboratory support and the animal house facility staff for technical assistance. Special gratitude is extended to Dr. Naomi Bisem, Dr. Geoffrey Kiptoo, and Dr. Stephen Barasa for their invaluable guidance throughout the study.

Conflicts of Interest

The authors declare no conflicts of interest.

References

- [1] Kerner, W. and Brückel, J. (2014) Definition, Classification and Diagnosis of Diabetes Mellitus. *Experimental and Clinical Endocrinology & Diabetes*, **122**, 384-386. <https://doi.org/10.1055/s-0034-1366278>
- [2] Zheng, Y., Ley, S.H. and Hu, F.B. (2018) Global Aetiology and Epidemiology of Type 2 Diabetes Mellitus and Its Complications. *Nature Reviews Endocrinology*, **14**, 88-98. <https://doi.org/10.1038/nrendo.2017.151>
- [3] Stumvoll, M., Goldstein, B.J. and van Haeften, T.W. (2005) Type 2 Diabetes: Principles of Pathogenesis and Therapy. *The Lancet*, **365**, 1333-1346. [https://doi.org/10.1016/s0140-6736\(05\)61032-x](https://doi.org/10.1016/s0140-6736(05)61032-x)
- [4] Asmat, U., Abad, K. and Ismail, K. (2016) Diabetes Mellitus and Oxidative Stress—A Concise Review. *Saudi Pharmaceutical Journal*, **24**, 547-553. <https://doi.org/10.1016/j.jsps.2015.03.013>
- [5] Giacco, F. and Brownlee, M. (2010) Oxidative Stress and Diabetic Complications. *Circulation Research*, **107**, 1058-1070. <https://doi.org/10.1161/circresaha.110.223545>
- [6] Padhi, S., Nayak, A.K. and Behera, A. (2020) Type II Diabetes Mellitus: A Review on Recent Drug Based Therapeutics. *Biomedicine & Pharmacotherapy*, **131**, Article ID: 110708. <https://doi.org/10.1016/j.biopha.2020.110708>
- [7] Erasto, P., Grierson, D.S. and Afolayan, A.J. (2007) Evaluation of Antioxidant Activity and the Fatty Acid Profile of the Leaves of *Vernonia Amygdalina* Growing in South Africa. *Food Chemistry*, **104**, 636-642.

- <https://doi.org/10.1016/j.foodchem.2006.12.013>
- [8] Nwanjo, H.U. (2005) Efficacy of Aqueous Leaf Extract of *Vernonia amygdalina* on Plasma Lipoprotein and Oxidative Status in Diabetic Rat Models. *Nigerian Journal of Physiological Sciences*, **20**, 39-42.
 - [9] Oboh, G. and Akinyemi, A.J. (2010) Inhibition of Key Enzymes Linked to Type 2 Diabetes and Sodium Nitroprusside-Induced Lipid Peroxidation in Rat Pancreas by Water Extract of *Vernonia amygdalina* Leaves. *Experimental and Toxicologic Pathology*, **62**, 613-620.
 - [10] Anwar, F. (2018) Phytochemical Screening Methods for Secondary Metabolites. *Journal of Pharmacognosy and Phytochemistry*, **7**, 1-5.
 - [11] Zohra, S.F., Meriem, B., Samira, S. and Muneer, M.A.S. (2012) Phytochemical Screening and Identification of Some Compounds from Mallow. *Journal of Natural Product and Plant Resources*, **2**, 512-516.
 - [12] Ayala, A., Muñoz, M.F. and Argüelles, S. (2014) Lipid Peroxidation: Production, Metabolism, and Signaling Mechanisms of Malondialdehyde and 4-Hydroxy-2-Nonenal. *Oxidative Medicine and Cellular Longevity*, **2014**, Article ID: 360438. <https://doi.org/10.1155/2014/360438>
 - [13] Kooti, W., Farokhipour, M., Asadzadeh, Z., Ashtary-Larky, D. and Asadi-Samani, M. (2016) The Role of Medicinal Plants in the Treatment of Diabetes: A Systematic Review. *Electronic physician*, **8**, 1832-1842. <https://doi.org/10.19082/1832>
 - [14] Vinayagam, R. and Xu, B. (2015) Antidiabetic Properties of Dietary Flavonoids: A Cellular Mechanism Review. *Nutrition & Metabolism*, **12**, Article No. 60. <https://doi.org/10.1186/s12986-015-0057-7>
 - [15] Tiwari, A.K. and Rao, J.M. (2002) Diabetes Mellitus and Multiple Therapeutic Approaches of Phytochemicals: Present Status and Future Prospects. *Current Science*, **83**, 30-38.
 - [16] Do, Q.D., Angkawijaya, A.E., Tran-Nguyen, P.L., Huynh, L.H., Soetaredjo, F.E., Ismadji, S., et al. (2014) Effect of Extraction Solvent on Total Phenol Content, Total Flavonoid Content, and Antioxidant Activity of *Limnophila aromatica*. *Journal of Food and Drug Analysis*, **22**, 296-302. <https://doi.org/10.1016/j.jfda.2013.11.001>
 - [17] Rena, G., Hardie, D.G. and Pearson, E.R. (2017) The Mechanisms of Action of Metformin. *Diabetologia*, **60**, 1577-1585. <https://doi.org/10.1007/s00125-017-4342-z>
 - [18] Patel, D.K., Kumar, R., Laloo, D. and Hemalatha, S. (2012) Diabetes Mellitus: An Overview on Its Pharmacological Aspects and Reported Medicinal Plants Having Antidiabetic Activity. *Asian Pacific Journal of Tropical Biomedicine*, **2**, 411-420. [https://doi.org/10.1016/s2221-1691\(12\)60067-7](https://doi.org/10.1016/s2221-1691(12)60067-7)
 - [19] Bonnefont-Rousselot, D. (2010) Metformin and Aging: Possible Mechanisms through Lipid Peroxidation and Antioxidant Enzyme Regulation. *Biogerontology*, **11**, 601-610.
 - [20] Maritim, A.C., Sanders, R.A. and Watkins, J.B. (2003) Diabetes, Oxidative Stress, and Antioxidants: A Review. *Journal of Biochemical and Molecular Toxicology*, **17**, 24-38. <https://doi.org/10.1002/jbt.10058>
 - [21] Ekor, M. (2014) The Growing Use of Herbal Medicines: Issues Relating to Adverse Reactions and Challenges in Monitoring Safety. *Frontiers in Pharmacology*, **4**, Article No. 177. <https://doi.org/10.3389/fphar.2013.00177>