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CCI, GMG, IOO, and CICO, developed the ideas and supervised the study; DMM, GMI, PSO, SOA, BT, JNS, and HNI, performed the experiments, collected data, and wrote the first draft of the manuscript; OAO performed the statistical analysis; BVA, OO, SA, COA, and HNI, reviewed the draft of the manuscript; all authors approved manuscript accomplishment.

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Evaluation of Antioxidant, Hypoglycemic and Hepatoprotective Effects of Leaf Extracts of *Artemisia annua* and *Vernonia amygdalina* in Alloxan Induced Diabetic Rats

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Abstract:

The global diabetes mellitus burdens and consequent combat approach has necessitated increased plant-based therapies. While non-fermented herbs and various synthetic drugs have been used, no sufficient success has been documented in the fight against this disease. The aqueous or non-fermented leaf extracts of *Artemisia annua* (A.AAQ) and *Vernonia amygdalina* (V.AAQ) and fermented leaf extracts of *A. annua* (A.AF) and *V. amygdalina* (V.AF) were evaluated for biochemical serum, lipid profile, in-vivo antioxidant parameters and body weight in alloxan induced diabetic rats. All extracts primarily V.AF and A.AF significantly decreased blood glucose levels ($p<0.001$). All extracts particularly A.AF, V.AF and A.AF+ V.AF significantly elevated Packed Cell Volume, Red Blood Cell Count, Hemoglobin Concentration, and Eosinophil levels ($p<0.05$; 0.001) but reduced Alanine phosphatase, Aspartate transaminase, Alkaline phosphatase and creatinine levels ($p<0.001$). Additionally, total cholesterol, Triglycerides and Low-density lipoprotein (LDL) were decreased ($p<0.05$; 0.01; 0.001), however, there was an increase in glutathione peroxidase (GPx) Protein, alongside a decrease in malondialdehyde (MDA) protein ($p<0.001$) in the diabetic rats. Body weights of diabetic rats significantly decreased ($p<0.01$; 0.001). In conclusion, the fermented extracts performed better in hypoglycemic activity in alloxan induced diabetic rats.

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INTRODUCTION

Diabetes is a metabolic disorder, characterized by elevated levels of blood sugar (Bakari *et al*., 2018). This results in high morbidity, economic and other burdens (Adeleye, 2021; Muhammad *et al.,* 2013). Several studies confirmed that plants can be used to treat various disorders (Ashraf *et al.,* 2020; Iqbal and Ashraf, 2018; Iqbal and Khalid, 2023; Ullah *et al.,* 2018; Zaynab *et al.,* 2018). Despite the advancement of various strategies in diabetes control, several authors have documented that *Artemisia annua* and *Vernonia amygdalina* possess the potency in diabetes management (Ogbonna *et al*., 2017). The fermented extract was more efficacious than the non- fermented extract except in the case of superoxide radical reduction assay where both fermented and non-fermented extracts performed well (Lee *et al*., 2019).

The pharmacological effects of *A. annua* and *V.amygdalina* are antioxidant, anti-inflammatory, antidiabetic, and antitumor, among others (Degu *et al.,* 2024; Lang *et al*., 2019; Messali *et al*., 2020; Talwar *et al.,* 2024). These activities are facilitated by the interplay of various phytochemicals like phenols, saponins, flavonoids, alkaloids, terpenes, etc in the plant extracts of *A.annua* and *V.amygdalina*. These plants display antidiabetic activity by various mechanisms such as upsurge in insulin discharge, reductions in hepatic glucose production, control of some enzymes used in carbohydrate metabolism such as α-glucosidase inhibitors, variation of certain regulation molecules such as PPARγ, hypolipidaemic activities, antioxidant effects (Helal *et al.,* 2014; Ogbonna *et al*., 2017; Axelle *et al*., 2020).

Phytochemicals like camphor, oleic acid, phytol, octadecanoic acid in *A.annua* and *V. amygdalina* may influence the reduction in blood glucose level, serum levels, of total glucose and total cholesterol, uric acid, creatinine and body weights. There was reduction ($p<0.01$) in serum insulin level and body weights after treatment of diabetic rats for 30 days twice daily with leaf extract of *A. annua*. This may have been facilitated by enhancement of pancreas's capacity to release insulin and perhaps even improve the work it performs (Helal *et al.,* 2014). There was significant reduction in blood glucose levels in High Fat Diet (HFD) + *A. annua* -fed mice relative to the HFD-fed mice ($P<0.05$). There was decrease in the body and liver weights in HFD-fed mice after treatment with *A. annua* ($P<0.05$) (Kim *et al*., 2016). Ttreatment of diabetic rats with *A. annua* resulted in a decrease in glucose level by 68.74% as well as a decrease in body weight and levels of Alkaline phosphatase (ALP), Aspartate aminotransferase (AST) and ALT compared with the normal control, diabetic control and standard control (Ogbonna *et al.,* 2017; Ejiofor *et al*., 2017).

There was a decrease in body weight, fasting blood glucose (494.84mg/dl to 81mg/dl on the 7^{th} day) and normalized the levels of total bilirubin, creatinine and HDL after treatment with 400mg/kg and 200mg/kg of the leaf extract of *V.amygdalina* on diabetic rats (Obarisiagbon *et al*., 2019). The impact of *V. amygdalina* extracts on diabetic rats showed decrease in the levels of ALP, AST, ALT, total cholesterol and regeneration of cells of the liver and kidneys relative to the control and standard drug used (Asante *et al.,* 2016; Ejiofor *et al.,* 2017).

This research is focused on assessing and comparing the effects of fermented and non-fermented leaf extracts of *A. annua* and *V. amygdalina* on serum biochemistry, in vivo-antioxidant and lipid profile associated with diabetes in rats.

MATERIALS AND METHODS

Study Area

The current work was performed in the General Biology Laboratory in the College of Biological

Sciences, Biochemistry Laboratory and Veterinary Teaching Hospital of Joseph Sarwuan Tarka University, Makurdi Benue State.

Collection and identification of plant materials

A. annua and *V. amygdalina* leaves were acquired from Centre for Biotechnology and Genetic Engineering (CBGE) University of Jos, Jos Plateau State and the farm behind Modern Market Makurdi, Benue State respectively. The *A. annua* var, chiknensis's batch number is PCN 004651/PAC4.8/CIC while the *V. amygdalina* was identified in the taxonomy unit in the Department of Plant Science and Biotechnology, Joseph Sarwuan Tarka University, Makurdi. Both plants were washed with uncontaminated water and dried indoors at room temperature.

Preparation of plant extract

A. annua and *V. amygdalina* powered leaves, each weighing 200g, were placed in separate flasks with 800ml of sterile condensed water each. The containers were subjected to heat using Bunsen burner for 120 seconds and cooled down to room temperature. These were aseptically filtered using Whatman filter paper (No1), then dried in a hot water bath, weighed, and stored at 5 °C in a refrigerator.

Preparation of fermented plant extracts

The boiled water was poured into a sterile flask, left for five minutes, and then poured into additional sterile bottles. Thirty millilitres of sterile distilled water were then placed into thermoses containing twenty grammes (20g) of the leaf extract. *A. annua* and *V. amygdalina* extracts were added to separate bottles containing ten (10) millilitres of 1.0 x 10^8 cfu/ml *S. cerevisiae* and *Lactobacillus acidophilus* culture, respectively. The bottles were corked, sealed, and stored in a dark environment for fourteen days without interruption. Draining the transparent portion into an additional sterile container was how racking was done after the allotted time. Seven more days were spent using the same process, and after a further fourteen days, the leftover mixture in the bottle was racked again.

After thirty five days, the fillings in the bottle were allowed to age for various evaluations.

Ethical approval

Ethical endorsement with a reference number BIO/UAM/21/009 was gotten from the College Research Ethical Committee of the College of Biological Sciences, Joseph Sarwuan Tarka University Makurdi.

Evaluation of antidiabetic activity of *A. annua* and *V. amygdalina* leaf extracts

Induction of Diabetes and Treatment

A single dose of 130 mg/kg bw of Alloxan was administered to the overnight fasted albino rats through intraperitoneal injection to induce diabetes. After 72hours of Alloxan administration, glucose levels were tested in the blood samples collected from the rats using Accu check Glucose Test Strips. Rats with fasting serum glucose levels above 7.8 mmol/dL were considered diabetic and selected for further studies (Asante *et al.*, 2016). Diabetic rats were treated orally, using the extracts for 14 days. Examination of blood glucose levels was done after treating the rats with the extracts. Rat blood was collected intravenously from the tip of the rat tail.

Experimental design

Animals were randomly divided into nine (9) groups. Each group had 3 rats.

Group 1 (Normal control): Non Alloxan induced rats. Group 2 (Negative control), Alloxan induced diabetic rats untreated. Group 3 (Standard control) Alloxan induced diabetic rats: Treated with a Standard drug (Glibenclamide). Group 4: Aqueous or non-fermented leaf extracts of *A. annua* (A.AAQ). Group5: Aqueous or non-fermented leaf extracts of *V. amygdalina* (V.AAQ). Group 6: Aqueous or non-fermented leaf extracts of *A. annua* (A.AAQ) + Aqueous or non-fermented leaf extracts of *V. amygdalina* (V.AAQ). Group 7: Fermented leaf extracts of *A. annua* (A. AF) . Group 8: Fermented leaf extracts of *V. amygdalina* (V. AF). Group 9: Fermented leaf extracts of *A. annua* (A. AF) +

Fermented leaf extracts of *V. amygdalina* (V. AF).

Evaluation of body weight Gain

The rats were regularly weighed to determine potential weight gain for a period of 14 days (Seller *et al.,* 2007).

Evaluation of effect of extracts on the lipid profile of blood plasma

The total cholesterol level was evaluated using enzymatic techniques by employing cholesterol ester/oxidase. The HDL content was assayed in the floating portion after precipitation of the LDL using phosphotungstic acid and $MgCl_2$. The values were calculated using Freidewald's formula (Freidewald *et al.,* 1972) as follows:

[LDL-chol] =[Totalchol]-[HDL-CHOL]-[[TG]/2.2

The triglycerides level was evaluated enzymatically by hydrolysis with lipoprotein lipase inside of glycerol, followed by glycerol phosphate and finally by dihydroxyacetone phosphate and H_2O_2 which in the presence of peroxidase was changed to amino phenazone. The urea was assessed in the presence of urease, to form CO_2 and NH_3. Phenol-hypo chloride was added to form an indophenol-blue compound with absorbance at 600nm. To evaluate Creatinine level, its reaction with pyric acid in alkaline buffer which resulted in a yellow-orange compound was observed and recorded. The color intensity evaluated at 500nm was relative to the creatinine content in the blood sample. Total protein was assayed using biuret reagent.

Evaluation of the *in vivo*- antioxidant effect of extracts on the blood plasma

The ability of plasma to eliminate DPPH radicals was evaluated using a modified method (Hasani *et al.,* 2007). A 50 µL of plasma was poured into 1250µL of Mehanolic DPPH solution (2.4 mg / 100 mL methanol) and incubated for about 30 minutes in the dim or dark place and centrifuged at 3,000 RPM for 20 minutes. The absorbance was measured at 517nm. The plasma antioxidant capacity was there after computed using the equation below:

Radical scavenging activity %) = {(Ablank – Asample) / Ablank} x 100.

Assessment of lipid peroxidation

Lipid peroxidation was evaluated by measuring the production of malondialdehyde (MDA) (Ohkawa *et al*., 1979).

The final byproduct of lipid peroxidation, malondialdehyde (MDA), is a useful indicator of oxidative stress and damage caused by free radicals. This technique's basic idea is that MDA and thiobarbituric acid (TBA) combine in an acidic environment and at a higher temperature (90–100°C) to produce pink MDA-(TBA) 2 complexes, which may be measured spectrophotometrically at 530 nm. One millilitre of 0.67% TBA was added after 0.5 millilitres of 20% TCA and 0.5 millilitres of tissue homogenate were combined. After 15 minutes of incubation at 100°C in a water bath, the mixture was cooled, 4 mL of n-butanol was added, and it was centrifuged for 15 minutes at 3000 rpm.

A spectrophotometric measurement of the absorbance of the clear pink supernatant at 532 nm was then made in comparison to a blank. MDA concentration is measured in nmol/g of tissue.

Evaluation of reduced glutathione (GSH)

This was performed according to the protocol of Ellman (1959). The concept was based on the fact that GSH is oxidised by 5, 5'-dithiobis (2-nitrobenzoic acid) (DTNB), which then reacts with glutathione (GSH) to produce 2-nitro-5-thiobenzoic acid (TNB), which has a yellow color. Thus, absorbance at 412 nm was used to measure GSH content. 10 mL of phosphate buffer (0.1 M, pH 8) was used to dilute 50 µL of the tissue homogenate. 20 µL of DTNB (0.01 M) was added to 3 mL of the dilution mixture. At 412 nm, absorbance was measured in comparison to a blank that was made in the same way. The GSH concentrations were measured using a calibration curve of GSH under the same conditions and were expressed in µ mol/g of tissue.

Evaluation of catalase activity

This was performed using the protocol of method of Claiborne (1985). The standard is established on the hydrogen peroxide H_2O_2 breakage by enzyme action based on the following reaction:

$2H_2O_2 \rightarrow 2H_2O + O_2$

The reaction mixture comprised 16.5 uL of tissue homogenate, 19 mM H_2O_2, and 50 mM potassium phosphate buffer with a pH of 7.4. After one minute of spectrophotometric monitoring of H_2O_2 degradation at 240 nm, the enzyme activity was computed using the formula:

K = 2.303/T x log (A1/A2)

Where: K: Rate of reaction; T: Time interval (minutes); A1: Absorbance at time zero; A2: Absorbance at 60 seconds interval

The enzyme activity of CAT was calculated by K/n in terms of units per milligram of protein (U /mg protein); where n is protein content.

Statistical analysis:

Data obtained were analyzed by means of R-Studio software and expressed as mean ± Standard Error of Mean (SEM). The Analysis of variance (ANOVA) was used to equate the means of all parameters with exception of glucose level in diabetic rats, where t-test was used. Statistical significance was established at $p<0.05$ and LSD was used to separate the means.

RESULTS AND DISCUSSION

The total cholesterol and triglycerides level were not much affected by both extracts alone, however, A.AF+ V.AF significantly decreased the LDL ($P<0.05$) while A.AAQ significantly raised the HDL level ($P<0.05$) (Table 1).

The general significant reduction in cholesterol, triglycerides and LDL and the increase in HDL levels due to the combination of the extracts fermented *A. annua* + *V. amygdalina* could be as a result of synergy between the two extracts used in the treatment of the diabetic rats. The presence of phytochemicals in a mixture of extracts in synergy may be responsible for the lowering of the cholesterol level. Phytochemicals are able to cut food consumption and auto synthesis of cholesterol, obstruct emulsification and esterification of cholesterol including the elimination of bile acid or relocation of cholesterol. Furthermore, there is evidence documented reports that, day-to-day application of the extracts to rats can result in decrease in the lipid profile in comparison to the control rats (Alara *et al*., 2017).

Table 1. Effects of the leaf extracts of *A. annua* and *V. amydgdalina* on Lipid Profile parameters of diabetic rats (mg/Dl).

Group	T. Cholesterol mg/dl	Triglycerides mg/dl	HDLmg/dl	LDLmg/dl
Normal control	119.20±9.62^{cd}	122.17± 6.8 ^{cd}	24.57± 1.5	70.37±11.6^{bc}
Diabetic control	133.90±9.01^{a}	127.03± 6.44^{bc}	20.83± 1.89	87.27± 7.37^{a}
Standard Control	122.77±6.05^{bcd}	118.63± 5.79d	23.00± 1.73	75.70±6.96^{abc}
A.AAQ	128.37±2.58^{abc}	133.30± 4.06^{ab}	25.47±O.70	80.23±7.21^{ab}
V.AAQ	130.70±10.27^{d}	137.13± 6.44^{e}	22.37± 2.38	80.97±7.21^{bc}
A.AAQ+V.AAQ	114.00±10.27^{ab}	109.73± 6.44^{a}	21.63±2.38	70.20±12.30^{ab}
A.AF	125.50± 0.12^{abc}	120.80±0.25^{cd}	22.47±0.24	78.90±o.35^{ab}
V.AF	120.00±0.21^{bcd}	114.57±o.31de	23.13±0.43	74.63±0.32^{abc}
A.AF+ V.AF	113.50±0.34^{d}	109.10±o.21^{e}	24.90±0.01	62.87±0.37^{c}
LSD	10.95	8.13		13.19
P-Value	<0.01	<0.001	>0.05	<0.05

Values are mean and standard error of means (Mean ±SEM) of three replicates. Mean values with superscripts down the column showed significant difference ($p<0.05$; 0.01; 0.001).
Mean values without superscript down the column are not significantly different (>0.05)

Our results showed that 200 mg/kgbw of A.AAQ and A.AAQ+V.AAQ significantly diminished the GP Protein ($P<0.05$) compared to the control groups. A.AAQ also caused a significant slash in SOD and MDA ($P<0.05$). Conversely, there was no significant difference ($P>0.05$) on catalase (Table 2).

In-vivo antioxidant effects of the extracts on diabetic rats which showed no significant increase in SOD U/mg Protein and Catalase, but there was significant increase in GPxU/mg Protein, and decrease in MDA U/mg protein due to the activity of the extracts of fermented *A. annua,* fermented *V. amygdalina* as well as by fermented *A. annua +V. amygdalina* may be linked to the extracts and the synergistic interactive effects between the bioactive components released in the process of fermentation and which are contained in the extracts. Such bioactive components include flavonoids, polyphenols, tannins etc which may have exerted scavenging power over free radicals associated with metabolic diseases like diabetes (Khan *et al.,* 2021). Lee et al. (2019) and Ogbonna et al. (2017) affirmed that the enhanced antidiabetic efficacy of extracts when co-administered facilitate synergy through fine glucose regulation, oxidative stress reduction, insulin simulated action and probable cell regeneration. The serum superoxide dismutase (SOD), acts by regulating the mitochondria function by scavenging O_2 radicals via oxidation/reduction reaction rate through transition metal ions present at the active site. Catalase breaks the hydrogen peroxide molecules into one molecule of Oxygen and two molecules of water in two step reactions. This ameliorates the cycle between hyperglycaemia and the oxidative damage.However, the decrease in MDA u/mg protein was caused by some of the extracts especially by the non-fermented or aqueous *A. annua* (A.AAQ). The impact created here may not necessarily be associated with fermentation but perhaps due to the effect of phytochemicals present in the extracts. A decrease in MDA is decrease in free radicals' activity. A reduction in MDA may increase glutathione peroxidase (GPX) in rats treated with these extracts. The presence of phytochemicals reduces the level of MDA there by enhancing the decrease in glucose level (Khan *et al.,* 2021). Asianuba et al. (2024) documented the antioxidant activity by *Vernonia amygdalina* ethanol leaf extract in mice infected with rodent malaria parasites.

Table 2. Effects of the leaf extracts of *A. annua* and *V. amydgdalina* on Antioxidant parameters of diabetic rats.

Group	GPx U/mg Protein	SOD U/mg Protein	CATALASE U/ml	MDA U/mg Protein
Normal control	2.08±0.1^{a}	122.07±3.42	1.26±0.14	2.98±0.58^{ab}
Diabetic Control	1.87±0.17^{ab}	122.07±3.42	1.26±0.13	3.64± 0.75^{a}
Standard Control	2.07±0.28^{a}	118.93 ±4.92	1.10 ±0.05	3.06 ± 0.39^{ab}
A.AAQ	1.07±0.08^{c}	107.97±6.08	1.06± 1.10	1.59±0.26^{c}
V.AAQ	1.93 ±0.08^{ab}	118.30±7.15	1.06± 1.11	2.95±0.13^{ab}
A.AAQ+V.AAQ	1.52±0.15^{bc}	119.18±13.19	1.23 ±0.11	2.35 ± 0.10^{c}
A.AF	2.21±0.01^{a}	117.10 ±0.1	1.10 ±0.02	2.66 ±0.06^{b}
V.AF	2.11±0.03^{a}	125.0667 ±0.04	1.33±0.03	2.66 ±0.02^{b}
A.AF+ V.AF	2.20±0.02^{a}	125.3667 ±0.34	1.55±0.05	2.35 ±0.08^{bc}
LSD	0.48	11.00	0.31	0.77
P-Value	<0.001	>0.05	>0.05	<0.001

Values are mean and standard error of means (Mean ±SEM) of three replicates.
Mean values with superscripts down the column are significantly different ($p<0.001$).
Mean values without superscripts down the column are not significantly different ($p>0.05$).

Our results showed that A.AAQ and A.AAQ+V.AAQ significantly increased albumin but reduced ALT level. The former also significantly reduced creatinine and Urea levels. The extracts of V.AF, A.AF+ V.AF and V.AAQ significantly decreased AST and ALP (Table 3).

The fermented extracts of *A. annua*, *V. amygdalina* and *A. annua* +*V. amygdalina* produced significant reduction in serum biochemistry parameters such as albumin, ALT, AST, ALP, creatinine and Urea. The decrease in protein level in the diabetic or negative control rats may be due to protein degradation in the tissues and the bioconversion of glycemic amino acid to CO_2 and H_2O (Eluehike *et al*., 2022). Serum proteins levels are affected by hydration profile. Also, generally, any significant increase in albumin, ALT, AST and ALP levels may suggest a liver damage (Asante *et al*., 2016; Ogugua *et al*., 2017). In addition, reduction in albumin could be due to the extracts ability to increase glucose concentration which occurs due to loss of the normal feedback inhibition of gluconeogenesis in the liver followed by an increased breakdown of fats and proteins as well as conversion of glucogenic Amino acid to glucose (Qaid and AbDelrahman, 2016). Albumin is responsible for about 50% of the total serum protein level and is a major protein carrier which circulates in the blood stream. Consequently, albumin deficiency may mean liver defects due to infection. This decrease in albumin, ALT, ASL, and ALP could be linked to the activity of phenol and flavonoids in the extracts, which protect the liver from free radical attacks and associated damages (Parthasarathy and Prince, 2021).

Table 3. Effects of the leaf extracts of *A. annua* and *V. amydgdalina* on Biochemical Serum parameters of diabetic.

Group	T. Protein g/dl	Albumin g/dl	ALT u/l	AST u/l	ALP u/l	Creatinine mg/dl	Urea mg/dl
Normal Control	5.07±0.12	2.57±0.01^{c}	111.3±0.56^{a}	41.10±0.34^{bcd}	52.60±0.45^{c}	0.88±0.26^{bc}	33.90±0.22
Diabetic Control	4.73±0.10	2.17± 0.03^{d}	116.50±0.58^{a}	45.50±0.67^{b}	56.13±0.45^{bc}	1.07±0.01^{b}	44.63± 0.12
Standard Control	5.07±0.12	2.63±0.01^{c}	108.70±0.46^{a}	44.47±0.23^{bc}	53.93±0.34^{bc}	0.84±0.01^{bc}	34.53±0.34
A. AAQ	5.50±0.23	3.20±0.01^{c}	47.47±0.45^{c}	58.80±0.45^{a}	59.60±0.56^{b}	0.55±0.34^{c}	39.63±0.31
V. AAQ	5.23±0.25	2.7± 0.03^{c}	111.30± 0.65^{a}	41.03±0.32^{bcd}	42.67±0.32^{b}	9.53±0.03^{b}	41.03±0.05
A.AAQ+V.AAQ	6.10±0.10	3.63±0.03^{a}	58.53±0.52^{b}	63.27±0.43^{a}	67.47±0.32^{a}	1.0±0.32^{b}	42.57± 0.12
A. AF	4.7±0.01	2.20±0.04^{d}	113.90±0.67^{a}	41.87 ±0.11^{bcd}	52.50±0.34^{c}	0.98±0.01^{b}	42.57±0.11
V. AF	5.07±0.13	2.33±0.03^{cd}	113.10±0.75^{a}	41.87 ±0.11^{cd}	53.47±0.32^{bc}	0.81±0.45^{bc}	39.37±0.23
A. AF+V.AF	5.77±0.14	2.7 ±0.03^{c}	113.60±0.46^{a}	38.37±0.35^{d}	41.67±0.04^{d}	0.82±0.12^{bc}	37.53±0.11
SD		0.35	10.65	5.21	6.46	0.41	
P-Value	>0.05	<0.001	<0.001	<0.001	<0.001	<0.001	>0.05

Values are means and standard error of mean (Mean ±SEM) of three replicates.
Mean values with superscript down the column were significantly different (p<0.05).
Mean values without superscript down the column are not significantly different (p>0.05)

All extracts significantly decreased the body weight when compared to the control (P<0.01; 0.001) while single treatment with fermented *V. amygdalina* extract performed better than all other groups (Table 4).

Although all the extracts did not show significant difference in body weight of the diabetes treated rats the body weight maintenance may have been achieved through heat production, appetite suppression (satiety), blocking of glucose absorption (Tucci, 2010). The slight decrease in weight observed in some rats may not be unconnected with the ability of these extracts to release metabolites which enhanced the body's ability to increase metabolism and burn fats, there by resulting in reduction in body weight.

Table 4. Effect of extracts of *A. annua* and *V. amygdalina* on body weight of diabetic rats.

Group	Body weight of diabetic rats		t_value	p-value
	After induction	After 14 days		
Normal control	5.43 ± 0.03	5.82 ± 0.16	-5.03	< 0.01
Negative control	11.8 ± 0.2	12.91 ± 0.02	-10.68	< 0.01
Standard control	11.52 ± 0.03	7.05 ± 0.02	220.3	< 0.001
A.AAQ	8.97 ± 0.02	8.97 ± 0.02	281	< 0.001
V.AAQ	8.1 ± 0.1	4.91 ± 0.02	54.44	< 0.001
A.AAQ+ V.AAQ	8.7 ± 0.1	5.3 ± 0	58.89	< 0.001
A.AF	14.8 ± 0.1	10.86 ± 0.01	64.77	< 0.001
V.AF	13.6 ± 0.3	9.11 ± 0.17	47.07	< 0.001
A.AF+ V.AF	9.02 ± 0.02	7.87 ± 0.06	52.92	< 0.001

Values are means and standard deviation (Mean±SD) of three replicates. Mean values down the column are significantly different (p<0.01; 0.001)

CONCLUSION

Diabetes mellitus is a global challenge hence requires multidimensional approach, concerted, continuous and coordinated efforts in fruitful researches on plants in order to combat it. Exploring the fermentation technology to produce more viable, affordable, available, less toxic antidiabetic products should be encouraged in order to handle diabetes. In this work, although most extracts normalized the serum biochemistry, lipid profile and in vivo antioxidant in the diabetes treated rats, the AAF, VAF, AAF+VAF, extracts performed best by significantly normalizing those parameters compared to the standard drug (Glibenclamide) and other non- fermented extracts.

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CONFLICT OF INTEREST

Authors hereby declare that they have no conflict of interest.

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