Lipid Peroxidation, Lipid Profile Changes and Antioxidant Properties of the Combination of *Vernonia amygdalina* and *Ficus exasperata* on the Blood, Liver and Kidney of Alloxan-Induced Diabetic Rats

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Authors' contributions

This work was carried out in collaboration among all authors. Author UUJ initiated the research design and interpreted results and generated conclusion, manuscript editorial and carried out the statistical analysis of all results. Author ARO dealt with rats' managements to include induction, feeding and sacrificing; Author OO dealt with general procurement. Author UMC procured rats for the research as well as worked extensively in plant extractions and was a major contributor in fine-tuning research methodology and the writing of the manuscript. All authors read and approved the final manuscript.

Original Research Article

ABSTRACT

Background: The use of plants known to possess significant antioxidant activities have been widely recommended in the complementary and alternate system of medicine in the treatment of diabetes mellitus. Among the many plant used in Nigeria for the management of DM are *Vernonia amygdalina* and *Ficus exasperata*. This study was designed to assess the effect of the combination

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of the aqueous extract of *Vernonia amygdalina* and *Ficus exasperata* on blood glucose level, lipid profile, hepatic enzymes, lipid peroxidation and antioxidant status in alloxan-induced diabetes in rats.

Method: Twenty five rats were divided into five groups. Four groups were made diabetic by the intra-peritoneal administration of alloxan monohydrate (150mg/kg body weight) while the fifth group served as normal control. Serum, hepatic and renal concentrations of reduced glutathione (GSH) and thiobarbituric acid reactive substances (TBARS) as well as the catalase activity were determined. The blood lipid profile and some hepatic enzymes were also studied.

Result: The combined extract lowered lipid peroxidation, increase glutathione concentration and catalase activity in all the tissues of diabetic rats. The individual extract lowered the total cholesterol LDL-Cholesterol, coronary risk index (CRI), and atherogenic index (AI) while increasing the concentration of HDL cholesterol in alloxan-induced diabetic rats. Diabetes lowered hepatic enzymes' activities but the leaf extract significantly increased it.

Conclusion: It can be concluded that combination of the extracts showed additive effect on each other and it is highly recommended for the management of diabetes.

Keywords: Diabetes; lipid peroxidation; antioxidant; Vernonia amygdalina; Ficus exasperata.

ABBREVIATIONS

DM   : Diabetes mellitus
TBARS   : Thiobarbituric acid reactive substances
GSH   : Reduced glutathione
NDC   : Non diabetic control
DC   : Diabetic control
VA   : Vernonia amygdalina group
Fe   : Ficus exasperata group
VaFe   : Vernonia amygdalina and Ficus exasperata combination group
HDL   : High density lipoprotein
LDL   : Low density lipoprotein
VLDL   : Very low density lipoprotein
ALP   : Alkaline phosphatase
AST   : Aspartate aminotransferase
ALT   : Alanine aminotransferase
CVD   : Cardiovascular disease
CHD   : Coronary heart diseases
BW   : Body weight

1. INTRODUCTION

Diabetes mellitus (DM), one of the fastest growing metabolic disorders, is a threat to global public health. At least 422 million people above 18 years old worldwide had diabetes in 2015 [1]. This figure has definitely overtaken an earlier projection made in 2006 of about 366 million to be diabetic by the year 2030 [2]. DM is also not only an economic burden, but has over the years led to a drastic reduction in life expectancy. In spite of the presence of known antidiabetic medicines, remedies from plant materials have been advocated alongside lifestyle and dietary control [3,4].

Oxidative stress, a common associate of DM, has been known to be a result of increased production of free radicals and a reduction of antioxidant defense. Therefore, compounds with proven antioxidant properties would serve well as good anti-diabetic agents. Many traditional treatments have been recommended in the complementary and alternate system of medicine in the treatment of DM because they possess significant antioxidant activities [5,6]. Thus, plants are considered useful means of managing certain disorders such as atherosclerosis, coronary heart diseases, kidney disorders, venereal diseases, rheumatism, arthritis etc. [7-11]. Among the many plants used in Nigeria for the management of DM are *Vernonia amygdalina* and *Ficus exasperata*.

Vernonia amygdalina, popularly called bitter leaf for its characteristic bitter taste, is a shrub that is grown throughout the tropic. It is cultivated mainly for its nutritional values [12,13]. The leaf has found importance in the treatment of diabetes [14,15,16], tuberculosis, abdominal disorder, fever [17] and asthma [18]. The phytochemical constituents of *V. amygdalina* include saponin, sesquiterpenes, lactones, flavonoids [19], cardiac glycosides, alkaloids and polyphenols [4].

Ficus exasperata, locally called sandpaper leaf, is a plant used for treating various ailments. The sap is used to stop bleeding [20], treat sore eye, stomach ache and also used to ease childbirth [21,22].Various studies also show that *Ficus exasperata* have antimicrobial and blood pressure reducing potentials as well as anti-inflammatory and antipyretic properties [23]

Sonibare et al. [24] and Oyewole et al. [25] reported that aqueous extract of *F. exasperata* lowers plasma triglyceride in alloxan-induced diabetic rats. *F. exasperata* contains phytochemicals like flavanoids, alkaloids, tannins, saponins and cyanogenic glycosides [21].

In South-West Nigeria, diabetic patients are usually encouraged to drink aqueous extract from boiled leaves of both *V. amygdalina* and *F. exasperata* to provide superlative action in ameliorating the debilitating effect of the disease. Therefore, this study was designed to investigate the veracity of the popular claim of additive effect of the two plants in the management of the disease through the measurement of blood glucose level, lipid peroxidation, antioxidant defense, lipid profile and hepatic enzymes in alloxan-induced diabetes in rats.

2. MATERIALS AND METHODS

2.1 Plant Collection

Fresh leaves of *V. amygdalina* and *F. exasperata* were collected in and around the premises of the Faculty of Basic Medical Sciences, Olabisi Onabanjo University, Ikenne Remo, Ogun State. They were identified by Mr. Adesanya Olumide of the Botany Department of the same University. The leaves were air-dried to constant weight before extraction.

2.2 Preparation of Extract

Fifty grams of the dried and pulverized leaves of *V. amygdalina* and *F. exasperata* were separately boiled in 1litre of distilled water. After 20 minutes, the suspension was filtered and evaporated to dryness. A 5% (w/v) solution of the dried extract of each plant was made to produce the solution given to the rats by intubation of 0.25ml/100g bw.

2.3 Animals and Treatment

Twenty five albino rats of the Wister strain (90g-120g) were obtained from the disease-free stock of the Animal Unit of the Biological Sciences Department of the University of Agriculture, Abeokuta, Ogun State, Nigeria. The rats were housed in cages with plastic bottom and wire screen top at room temperature with a 12 hour light-dark cycle and adequate ventilation. The rats were weighed and acclimatized to animal house condition for one week and fed rat chow (Ladokun Feeds, Ibadan, Oyo State, Nigeria) and water *ad-libitum.*

After acclimatization, the rats were reweighed and fasted overnight. Fasting blood glucose level was determined with the aid of a glucometer (Accu-chek Active, Roche Diagnostics, Indianapolis, U.S.A). The rats were divided into five groups based on equalized mean blood glucose level. One group of rats was kept as the Non-diabetic control (NDC) group. Four of the five groups were made diabetic by the intraperitoneal administration of alloxan monohydrate (Sigma, St Louis, MO, USA) dissolve in normal saline at a concentration of 150mg/kg body weight of rat while the fifth group (kept as Non Diabetic Control (NDC) group) received equivalent amount of normal saline. The feed intake was recorded daily and the body weights were taken weekly. The cages were cleaned daily to maintain a proper hygienic condition for the rats.

After one week of alloxan administration, the pre-prandial blood glucose concentration was again determined. The rats with blood glucose concentration three to five times the initial blood glucose concentration of the rats prior to the administration of alloxan were considered diabetic. The diabetic rats were further divided into four groups based on equalized mean blood glucose level. The groups of rats were designated as:

1. Group 1- Non-diabetic control (NDC) group (Rats fed only rat chow).
2. Group 2- Diabetic control (DC) group (Diabetic rats fed rat chow as the NDC).
3. Group 3- *V. amygdalina* (Va) group (Diabetic rats fed rat chow but received oral administration of 0.25ml/100g bw/day of *V. amygdalina).*
4. Group 4- *F. exasperata* (Fe) group (Diabetic rats fed rat chow but received oral administration of 0.25ml/100g bw/day of *F. exasperata*).
5. Group 5- *V. amygdalina* and *F. exasperata* (VaFe) group (Diabetic rats fed rat chow but received oral administration of 0.25ml/100g bw/day made of 1:1 of *V. amygdalina* and *F. exasperata*).

The rats were managed for four weeks. Fasting blood glucose level was determined at the end of the experiment using a glucometer. The rats were killed after anesthesia with ether and the livers and kidneys were removed, weights were

recorded and organs were immersed in saline and stored at 4°C before use.

2.4 Biochemical Analysis

Fasting blood glucose level was determined with a glucometer (Accu-chek Active, Roche diagnostics, Indianapolis) after blood was drawn from the tail. Total cholesterol, triglyceride, alkaline phosphatase (ALP), alanine aminotransferase (ALT) and aspartate aminotransferase (AST) activities were determined using commercially available kits prepared by Cromatest® diagnostics (Joaquim Costal, Montgat, Barcelona, Spain). Tissue protein concentration was determined by the method of Lowry et al. [26]. Catalase activity was determined according to the method described by Tukahara et al. [27] where the rate of decomposition of hydrogen peroxide (H_2O_2) was measured at 570 nm. Reduced glutathione (GSH) was measured by the method of Sedlak and Lindsay [28] where protein bound sulfhydryl group in tissues was estimated with the Ellman reagent (5,5^I-dithionitrobenzoic acid). Lipid peroxidation in tissue homogenate was determined using the procedure of Okhawa et al. [29]. Lipid peroxidation was assessed as the amount of thiobarbituric acid reactive substances (TBARS) produced. High density lipoprotein (HDL) cholesterol was measured by first precipitating low density lipoprotein (LDL) cholesterol with phosphotungstate and magnesium and subsequently determining the amount of cholesterol in the supernatant. Very low density lipoprotein (VLDL) cholesterol was estimated as Triglyceride ÷ 5 and subsequently low density lipoprotein was calculated from the Friedwald equation [30].

LDL-cholesterol = Total cholesterol – (HDL-C + VLDL-C)

Atherogenic and coronary risk indices were calculated according to Nwagha et al. [31] as Log_{10} (TG/HDL-C) and coronary risk index as TC/HDL-C.

2.5 Statistical Analysis

All the results were expressed as mean ± SEM for five animals in each group. All the grouped data were statistically evaluated with SPSS 10.0 software. Hypothesis testing methods included one way analysis of variance (ANOVA) and subsequent comparisons between groups were made using Duncan's Multiple Range Test (DMRT). Statistical significance was set at $p < 0.05$.

3. RESULTS

Fig. 1 showed the blood glucose levels of the control and experimental rats before and after treatments with the various extracts. Before treatment, there was a significant increase ($p ≤ 0.05$) in the blood glucose level of the diabetic rats when compared with the NDC. However, administration of the extracts of V. *amygdalina* and *F. exasperata* and the combination significantly lowered ($p ≤ 0.05$) the blood glucose levels in the treated diabetic rats when compared with the untreated diabetic rats (DC). It should be noted that the *F. exasperata* treatment lowered the blood glucose more effectively than the V. *amygdalina* and the combination treatments.

Fig. 2 showed the body weight changes of control and experimental rats. There was no significant difference ($p ≤ 0.05$) in the initial body weights of the control and experimental rats. However, a significant decrease ($p ≤ 0.05$) in final body weight of the diabetic rats was observed in the diabetic rats when compared with the control. However, administrations of the extracts lead to significant increase ($p ≤ 0.05$) in body weight although the increase in weight was significantly lower still when compared with the NDC.

Tables 1, 2 and 3 showed the catalase activity as well as the concentration of thiobarbituric acid reactive substances (TBARS) and reduced glutathione (GSH) in the blood, liver and kidney of control and experimental. The catalase activity was significantly reduced ($p ≤ 0.05$) in the diabetic rats when compared with the NDC whereas administration of the aqueous extract of V. *amygdalina* and *F. exasperata* as well as the combination of the extracts significantly increased ($p ≤ 0.05$) the catalase activities in the blood and in the kidney. Meanwhile, the extract effectively restored the catalase activity to normal in the liver as there was no significant difference ($p ≤ 0.05$) in the catalase activity of the NDC and the extract treated groups of diabetic rats. A significant increase ($p ≤ 0.05$) in TBARS concentration was observed in the diabetic rats when compared with the NDC. However, administrations of the extract significantly reduced ($p ≤ 0.05$) the TBARS level. The GSH level was significantly reduced in the diabetic rats compared with the NDC. However, administration of the aqueous extract of V. *amygdalina* and *F. exasperata* as well as the

combination of the extracts lead to a significantly increase (p≤0.05) the GSH level. In all the tables, there was no significant difference (p≤0.05) in values of the VaFe group when compared with the Va or Fe group.

Table 4 showed the lipid profile and the Coronary Risk Index (CRI) and the Atherogenic Index (AI) in the control and experimental rats. The total cholesterol was significantly increased (p≤0.05) in the DC group when compared with the control while the extracts treated groups show no significant difference (p≤0.05). Triglyceride level was significantly increased (p≤0.05) in all the diabetic groups when compared with the control. Treatment with extract of *F. exasperata* was able to lower the triglyceride level in the diabetic rats as the triglyceride level was significantly lower (p≤0.05) when compared with the NDC but treatment with the extract of *V. amygdalina* was not able to lower the triglyceride level of the diabetic rats. HDL-cholesterol was significantly reduced (p≤0.05) in the diabetic rats when compared with the control. The highest significant increase was observed in the diabetic

untreated (DC) group. The LDL-cholesterol and VLDL cholesterol were increased significantly (p≤0.05) in the diabetic groups of rats. Diabetic rats treated with extracts of V. *amygdalina* and F. *exasperata* showed no significant difference (p≤0.05) in the CRI when compared with the normal (NDC) rats. However, there was a significant increase (p≤0.05) in the CRI of the diabetic untreated (DC) rats when compared with the NDC. Atherogenic index (AI) was significantly higher (p≤0.05) in the diabetic rats when compared with the NDC. The highest significant increase was however observed in the DC group.

Fig. 3 showed the activities of alanine aminotransferase, aspartate aminotransferase and alkaline phosphatase in the livers of control and experimental rats. The ALT, AST and ALP activities were significantly reduced (p≤0.05) in the diabetic rats when compared with the NDC. However, administration of the extracts (Va, Fe and VaFe) significantly increased (p≤0.05) the levels of the various enzymes in the livers of the various treated diabetic groups when compared with the NDC.
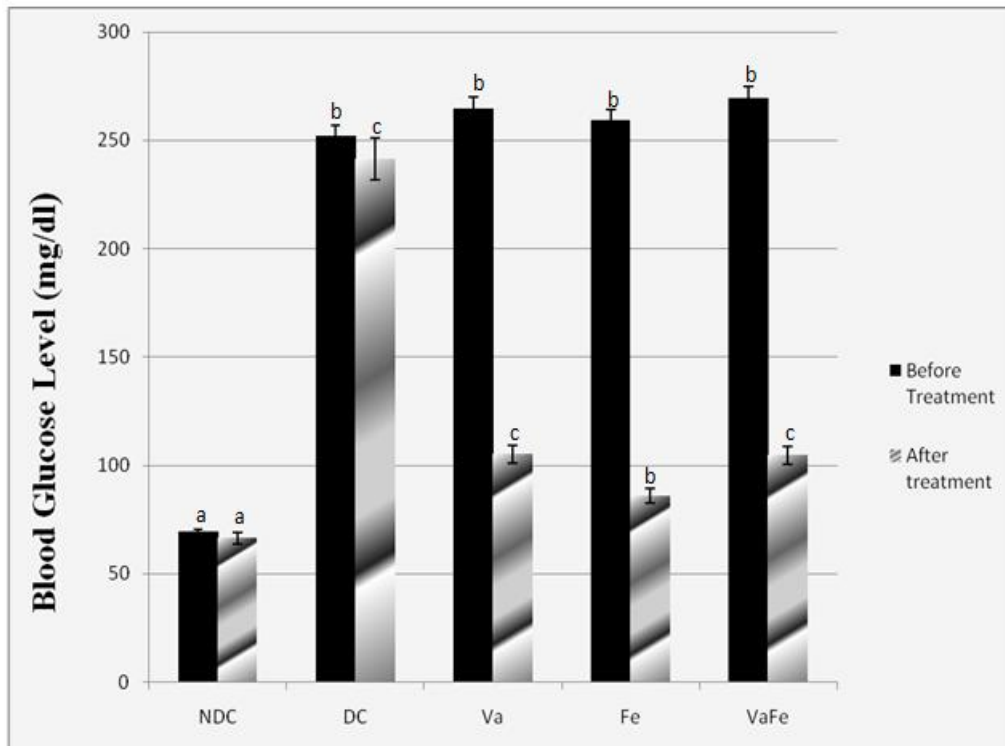

Fig. 1. Blood glucose level of control and experimental rats
Values are expressed as mean ± SEM. Mean values are compared using One-Way ANOVA. Level of significance was evaluated using Duncan's Multiple Range Test (DMRT) at p≤0.05. Bars the same alphabet are not significantly different (p≤0.05)
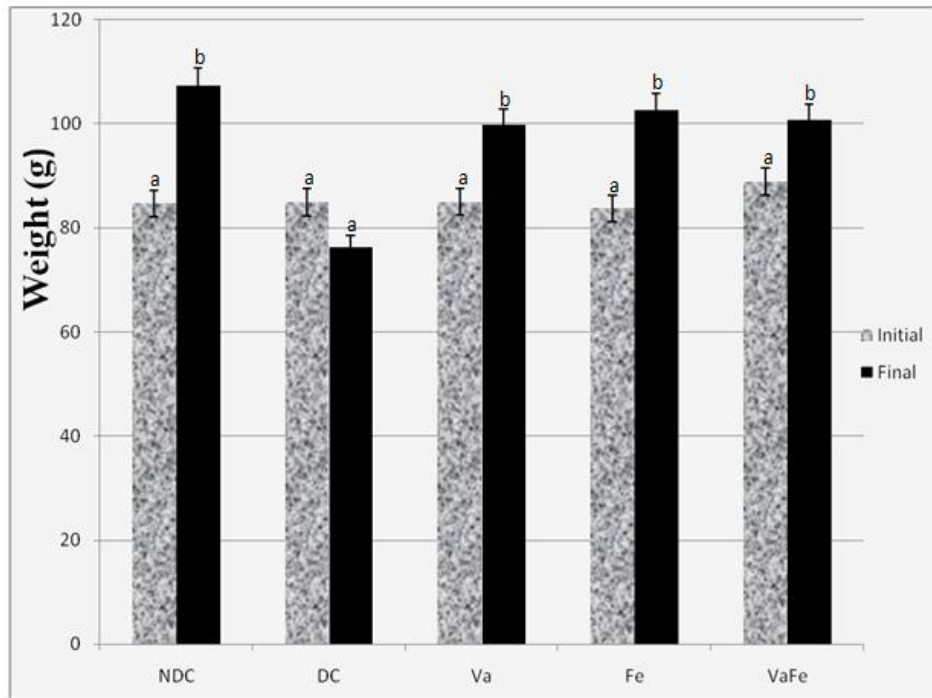
Fig. 2. Body weight changes of control and experimental rats
Values are expressed as mean ± SEM. Mean values are compared using One-Way ANOVA. Level of significance was evaluated using Duncan's Multiple Range Test (DMRT) at p≤0.05. Bars of the same colour with the same alphabet are not significantly different (p≤0.05)
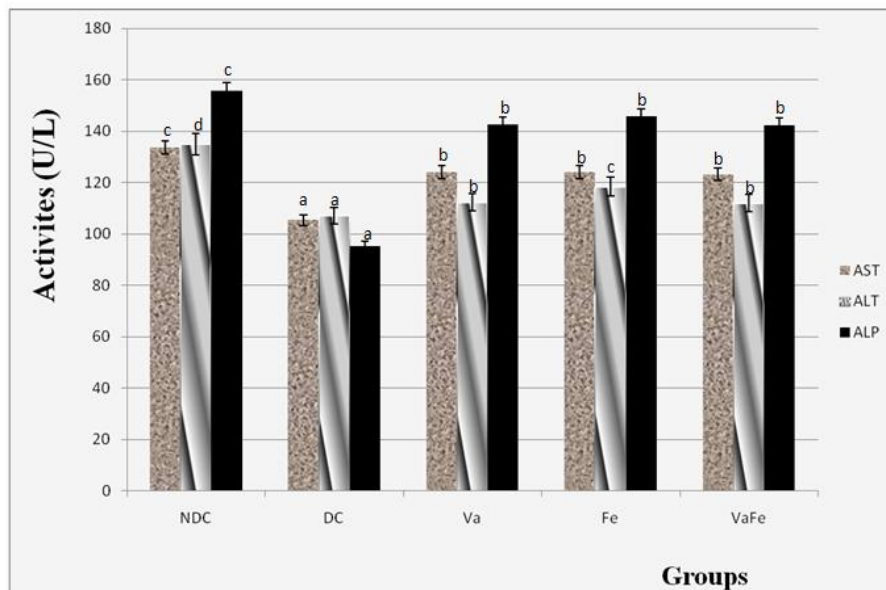

Fig. 3. Hepatic alanine and aspartate aminotransferases and alkaline phosphatases activities of control and experimental rats
Values are expressed as mean ± SEM. Mean values are compared using One-Way ANOVA. Level of significance was evaluated using Duncan's Multiple Range Test (DMRT) at p≤0.05. Bars of the same colour with the same superscript are not significantly different (p≤0.05)

Table 1. Serum TBARS, GSH and catalase activity of control and experimental rats

	TBARS (mM/dl)	GSH (mg/dl)	*Catalase (U/mg protein)
NDC	51.84 ± 0.60[a]	46.20 ± 3.56[b]	3.71 ± 0.10[c]
DC	105.05 ±1.65[d]	16.04 ± 1.73[a]	1.94 ± 0.07[a]
Va	65.79 ± 0.44[c]	43.90 ± 3.30[b]	3.08 ± 0.05[b]
Fe	59.24 ± 0.94[b]	41.10 ± 1.76[b]	3.07 ± 0.06[b]
VaFe	57.14 ± 0.65 [b]	43.58 ± 2.35[b]	3.04 ± 0.05[b]

*Values are expressed as mean ± SEM. Mean values are compared using One-Way ANOVA. Level of significance was evaluated using Duncan's Multiple Range Test (DMRT) at p≤0.05. Values in the same column with the same superscript are not significantly different (p≤0.05); *Unit of catalase activity is expressed as the µmoles of hydrogen peroxide decomposed per minute per mg of protein*

Table 2. Hepatic TBARS, GSH and catalase activity of control and experimental rats

	TBARS (mM/100g tissue)	GSH (mg/100g tissue)	*Catalase (U/mg protein)
NDC	51.50 ± 0.48[a]	49.64 ± 0.75[c]	3.66 ± 0.08[b]
DC	104.11 ± 0.75[d]	27.17 ± 1.26[a]	2.01 ± 0.04[a]
Va	62.03 ± 0.58[c]	44.63 ± 1.11[b]	3.61 ± 0.11[b]
Fe	61.94 ± 0.46[bc]	42.17 ± 0.94[b]	3.43 ± 0.09[b]
VaFe	57.11 ± 0.50[b]	43.29 ± 1.08[b]	3.58 ± 0.12[b]

*Values are expressed as mean ± SEM. Mean values are compared using One-Way ANOVA. Level of significance was evaluated using Duncan's Multiple Range Test (DMRT) at p≤0.05. Values in the same column with the same superscript are not significantly different (p≤0.05); *Unit of catalase activity is expressed as the µmoles of hydrogen peroxide decomposed per minute per mg of protein*

4. DISCUSSION

Alloxan-induced diabetes is characterized by severe weight loss and. Noori and Kopple [32] suggested that this could be as a result of protein wasting due to unavailability of carbohydrate for utilization as energy source. Administration of the extracts (Va, Fe, and VaFe) controlled this weight loss to a considerable level although the body weight remained lesser than the NDC's. The treatments bring about a decrease in blood sugar level and thus enhanced body weight. The possible mechanism by which *V. amygdalina, F. exasperata* and their combination bring this about could be either by increasing insulin secretion in the Islet of Langerhans or by potentiating the responsiveness of insulin to blood glucose [33]. It has also been suggested that this could be as a result of the ability of the extract of *V. amygdalina* to inhibit the eenzymes α-glucosidase and α-amylase (enzymes that catalyze the hydrolysis of α-1,4-glycosidic linkages in polysaccharides), so that it functions to reduce post-prandial hyperglycemia [34,35].

Oxidative stress has been known to be a major factor in the pathogenesis of diabetes. Free radicals are formed by glucose degradation, glucose auto-oxidation and protein glycation [36]. The free radicals produced react with polyunsaturated fatty acids in the cell membranes leading to lipid peroxidation subsequently leading to the formation of more free radicals [37,38]. Thiobarbituric Acid Reactive substances (TBARS), known as markers for lipid peroxidation was significantly increased in the diabetic rats. Thus, this shows that hyperglycemia leads to an increase in lipid peroxidation in the tissues. TBARS level was however significantly lowered in the treated diabetic rats compared with the untreated diabetic rats. This suggests that the extracts may possess lipid peroxidation inhibitory properties. However, the inhibitory property/(ies) and the nature of the inhibition are not fully known.

Antioxidants play important role in scavenging free radicals produced under oxidative stress [39,40]. In the present study, the concentration of glutathione, an antioxidant which is a direct scavenger of free radical as well as substrate for glutathione peroxidase [41,42], was significantly reduced in the diabetic rats. The treatments with the extracts lead to an increase in the GSH levels. The possible mechanism by which the extract exhibit this property could be by enhancing the synthesis of GSH or/and by reducing free radicals production hence less utilization of endogenous GSH.

Catalase is a hemoprotein which serves as an antioxidant. It catalyzes the reduction of hydrogen peroxide and protects tissues from reactive hydroxyl radicals [42]. In the present

Table 3. Renal TBARS, GSH and catalase activity of control and experimental rats

	TBARS (mM/100g tissue)	GSH (mg/100g tissue)	*Catalase (U/mg protein)
NDC	43.79 ± 1.40[a]	44.50 ± 2.02[c]	3.88 ± 0.08[c]
DC	116.99 ± 2.48[c]	21.37 ± 2.53[a]	1.98 ± 0.04[a]
Va	66.59 ± 1.40[b]	35.57 ± 1.73[b]	2.98 ± 0.06[b]
Fe	63.91 ± 2.53[b]	35.71 ± 2.61[b]	2.75 ± 0.08[b]
VaFe	61.41 ± 2.04[b]	36.38 ± 2.83[b]	3.22 ± 0.08[b]

*Values are expressed as mean ± SEM. Mean values are compared using One-Way ANOVA. Level of significance was evaluated using Duncan's Multiple Range Test (DMRT) at p≤0.05. Values in the same column with the same superscript are not significantly different (p≤0.05); *Unit of catalase activity is expressed as the µmoles of hydrogen peroxide decomposed per minute per mg of protein*

Table 4. Lipid profile and Coronary Risk Index (CRI) and Atherogenic Index (AI) of control and experimental rats

	Total Cholesterol (mg/dl)	Triglyceride (mg/dl)	HDL-C (mg/dl)	LDL-C (mg/dl)	VLDL-C (mg/dl)	Coronary risk index	Atherogenic index
NDC	147.75± 2.13[a]	69.96 ± 0.77[a]	108.21± 2.20[c]	25.33 ± 0.49[a]	13.98 ± 0.48[a]	1.37 ± 0.05[a]	0.23 ± 0.007[a]
DC	162.47 ± 3.02[b]	88.65 ± 1.33[c]	65.16 ± 3.58[a]	80.09 ± 1.57[c]	18.07 ± 0.45[c]	2.49 ± 0.08[b]	1.23 ± 0.011[c]
Va	141.99± 4.10[a]	86.38± 1.19[c]	95.36 ± 4.06[b]	29.76 ± 0.28[b]	17.05 ± 0.57[bc]	1.49 ± 0.04[a]	0.31 ± 0.009[b]
Fe	145.34± 1.35[a]	84.39 ± 1.03[b]	97.72 ± 1.18[b]	30.91 ± 0.63[b]	16.88 ± 0.31[b]	1.49 ± 0.06[a]	0.32 ± 0.009[b]
VaFe	141.02 ± 3.06[a]	86.82 ± 0.85[bc]	95.73 ± 3.25[b]	29.73 ± 0.25[b]	17.36 ± 0.47[bc]	1.47 ± 0.08[a]	0.31 ± 0.008[b]

Values are expressed as mean ± SEM. Mean values are compared using One-Way ANOVA. Level of significance was evaluated using Duncan's Multiple Range Test (DMRT) at p≤0.05. Values in the same column with the same superscript are not significantly different (p≤0.05).

study, catalase activity was significantly reduced in the diabetic rats. This reduction could possibly be as a result of catalase inactivation by glycation or exhaustion by hydroxyl radicals [43]. The treatments by the extracts increased the catalase activity. This could mean that the extract inhibit glycation of catalase in diabetes or/and reduced hydroxyl radical production or/and improve the activity of the antioxidant enzyme.

Changes in the serum lipid profiles are usual occurrence in diabetes [44] and these are likely to increase the risk of coronary heart diseases (CHD). In this study, a significant increase in the level of LDL-cholesterol and VLDL-cholesterol was observed in the diabetic rats. Emphasis has been given that elevated level of LDL-C and VLDL-C are important factors for CHD and lowering their levels has been shown to reduce the progression of CHD [45]. In this study, the various extracts effectively lowered the levels of LDL-C and VLDL-C.

Atherogenicity with its associated cardiovascular diseases is a major cause of death around the world. In the past, plasma total cholesterol has received much importance because of its strong and consistent correlation with atherosclerosis and CHD. However, it has been shown that the LDL-C/HDL-C ratio is a stronger determinant of atherogenicity of the lipoproteins rather than the lipid profile of the individual lipoprotein fraction [46]. In the present study, diabetes leads to an increase in the atherogenic index. However, administration of the extracts effectively lowered the ratio. This is because of the inverse relationship between HDL-C level and CVD/CHD which has also been documented [47]. This study shows a significant decrease in the HDL-C level in the diabetic rats. However, the extracts were able to increase the level of HDL-C in the serum. This indicates the extracts could lead to a reduced risk of atherosclerosis and CHD associated with diabetes.

Serum alkaline phosphatase, alanine aminotransferase and aspartate aminotransferase activities determination are parameters usually used in the diagnosis of hepatocyte necrosis and damage [48]. Increased level of these markers in the serum is usually indicative of a disease liver. However, increased level of these biomarkers could mean a decreased level in the liver. The decreased level of these enzymes in the diabetic rats could be as a result of loss of hepatic integrity due to the effect of excess free radicals and lipid peroxidation. The extracts may have prevented the increase in free radicals, ensured antioxidative protection of the liver and, these in turn, prevented lipid peroxidation of the organ.

5. CONCLUSION

It can be concluded that both the *V. amygdalina* and *F. exasperata* are very effective in the management of diabetes viz in controlling lipid peroxidation and protecting the hepatic tissue from oxidative damage. It is also imperative to note that the combination of the extracts showed no significant difference from singly administering of individual extract. However, the anomalous blood glucose levels of the various treatments require further study. It is also imperative to identify the various active components of both *V. amygdalina* and *F. exasperata* that elicit these sterling antioxidant properties that make them effective in the management of diabetes.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

ETHICAL APPROVAL

Animal Ethic committee approval has been taken to carry out this study.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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