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Role of *Vernonia Amygdalina* on Plasma Lipid Profile, Liver and Kidney Enzymes in Rats with Streptozotocin-Induced Diabetes

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Abstract

Diabetes mellitus is a non-communicable disease which has been associated with liver and kidney injuries, and at the same time affects lipid profiles. The aim of this study was to investigate the role of *Vernonia amygdalina* (VAM) on plasma lipid profile, liver and kidney enzymes in rats with streptozotocin -induced diabetes. Twenty-five male albino wistar rats weighing between 137 and 223 g were randomly grouped into five of five rats per group as follows: control, diabetic, diabetic + metformin (MET), diabetic + VAM at 150, 300 mg/kg. Diabetes was induced by administration of 45 mg/kg body weight streptozotocin (STZ) dissolved in citrate buffer (0.01 M, pH 4.5) by single intraperitoneal injection. Three days after, when diabetes was confirmed, MET and VAM were administered daily by oral gavage for 7 days. Animals were fasted overnight after the last administration of MET and VAM, sacrificed, blood was collected and plasma prepared for lipid profile estimation. Liver and kidney were collected, weighed, homogenized and supernatants obtained for enzymes and biochemical assays. There were no significant ($p>0.05$) change in the weights of animal, liver and kidney, liver/rat and kidney/rat ratios, plasma cholesterol (CHOL) concentration, activities of liver and kidney aspartate aminotransferase (AST), alanine aminotransferase (ALT), liver gamma-glutamyl transferase (GGT), lactate dehydrogenase (LDH), and liver and kidney total protein (TPRO) concentrations; significant ($p<0.05$) decrease in triglyceride (TRIG), high density lipoprotein-cholesterol (HDL), low density lipoprotein-cholesterol (LDL), very low density lipoprotein-cholesterol (VLDL); and significant ($p<0.05$) increase in fasting blood glucose (FBG) level, kidney GGT, LDH activities, liver and kidney creatinine (CREA) and total bilirubin (TBIL) concentrations of diabetic (STZ) rats compared with normal control. The treatment of the diabetic rats with MET and VAM significantly modulated positively these parameters compared with the diabetic rats. This study further explains the protective role played by VAM in dyslipidaemia, liver and kidney injuries resulting from diabetes.

Keywords: Vernonia amygdalina; Diabetes; Lipid profile; Hepatic and renal enzymes; Streptozotocin.

1. Introduction

Diabetes mellitus (DM) is one of the major non-communicable diseases. It is as a result of a high glucose concentration in the blood otherwise known as hyperglycaemia. Recently, the World Health Organization (WHO) noticed that the global prevalence of diabetes has been rising rapidly in low- and middle-income nations than the high-income ones [1]. The estimated death caused directly by diabetes in 2016 was 1.6 million and in 2012, 2.2 million death was attributed to high blood glucose. The severity of diabetes has majorly cause blindness, heart attack, kidney failure, stroke and lower limb amputation [2-4]. Type 1, insulin-dependent diabetes mellitus (T1DM) and type 2, non-insulin-independent diabetes mellitus (T2DM) are the two main types of DM. T2DM occurs majorly in adults that is about 40 years old and above and is caused by a deficiency of insulin or its secretion [5]. Lifestyle factors such as unhealthy diet and lack of physical activity or exercise that may result in excess body weight and abdominal obesity, and also genetic factors are known causes of T2DM [1, 6].

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A complex metabolic disorder, metabolic syndrome (MS) is characterized by hypertension, hyperinsulinemia, dyslipidemia, obesity and T2DM [7]. Lipid abnormalities has been reported to be common in DM patients [8] and dyslipidaemia reported as one of the major risk factors for macrovascular complications in DM [9, 10]. Dyslipidemia in T2MD reportedly increased plasma triglyceride levels, elevated low density lipoprotein cholesterol (LDL-C) and total cholesterol but reduced high-density lipoprotein cholesterol (HDL-C) [9, 11]. The high level of triglyceride (hypertriglyceridemia) and low level of HDL result in increased fatty acids, which stimulate insulin resistance and cause β-cell dysfunction [12]. Hence, it is important to evaluate the lipid profiles when treating diabetes in order to control or avoid abnormalities resulting from hypertriglyceridemia and low HDL. Serum lipids elevation has been associated with a high risk of coronary heart disease (CHD) in diabetes patients as well as non-diabetes patients [13]. Investigations have also shown that diabetes is associated with complications in the renal system. Diabetic nephropathy (DN) is the only major cause of end-stage renal failure worldwide. DN is described as partial loss of kidney functions related to nephrotic syndrome, glomerulosclerosis, declining glomerular filtration rate (GFR), elevated arterial blood pressure, persistent albumin-urea and fluid retention [14]. The effect of glycogen accumulation in the kidney tubules which is the outcome of hyperglycemia is said to account for the DN disease progression [15]. The global rapid increase of DM has made DN the principal cause of end-stage renal disease. The role of the liver to regulate carbohydrate metabolism by using glucose as a major source of fuel has made the organ to be more susceptible to diseases of MS, especially DM [16]. The observed increase in liver size and weight, that is fatty liver in MS induced by high consumption of sugar that contribute to the nonalcoholic steatosis progression has been attributed to its connection to hyperlipidemia, obesity and diabetes [17]. Studies have shown that the occurrence of hepatic tissue damage in MS is through increased plasma concentrations of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) [17]. Other investigations have equally shown higher levels of liver enzymes (AST, ALT) and alkaline phosphatase (ALP) in T2DM patients than those with no DM [18-20]. The global increase in the liver injury-associated diabetes has become worrisome, more especially in developing countries where the disease is still not being well managed.

To manage and prevent T2DM and its associated complications in Nigeria and many African countries, majority of the diabetic patients use herbal concoctions prepared from medicinal plants with antidiabetic properties. One major plant use for this purpose in Nigeria is *Vernonia amygdalina*, and the hypoglycemic activity of the plant has been reported extensively. *V. amygdalina* is used in many countries to manage various diseased conditions such as malaria, intestinal worms, hypertension, sexual functionality, kidney disorders and liver disorders, among many others [21, 22]. Phytochemical screening of leaf extract of the plant revealed the presence of polyphenol, flavonoid, saponin, tannin, riboflavin, amino acids (glycine, cysteine and nicotinamide), sesquiterpene, sugar and oxalate [23, 24]. It contains useful minerals such as K+, Ca^{2+}, Na^{+}, P^{3-}, Mg^{2+}, Mn^{2+}, Fe^{2+}, Cu^{2+} and Zn^{2+} [23, 25]. Therefore, this study seeks to evaluate the role of *Vernonia amygdalina* on plasma lipid profile, hepatic and renal enzymes in rats with streptozotocin-induced diabetes.

2. Materials and Methods

2.1. Chemicals and Reagents

The assay kits used were products of Randox Laboratories, United Kingdom. These are aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyltransferase (GGT), lactate dehydrogenase (LDH), total cholesterol, triglyceride, high density lipoprotein-cholesterol (HDL), low density lipoprotein-cholesterol (LDL), very low density lipoprotein-cholesterol (VLDL), creatinine, total protein and total bilirubin. Drug and chemicals used include metformin, steptozotocin, chloroform, normal saline and others were of analytical grades from BDH, UK and Sigma-Aldrich, Germany

2.2. Collection of Plant Material

Fresh plants of *Vernonia amygdalina* was bought from a farm at a village, Imushin, Ogun State, Nigeria. It was duly identified and authenticated by Mr. Adeleke, Department of Pharmacognosy, College of Medicine of the University of Lagos, Nigeria.

2.3. Preparation of *V. Amygdalina* Extract

V. amygdalina fresh leaves were removed from the stalks of the plant, rinsed thoroughly in running tap water and air-dried at room temperature in the Departmental Laboratory for 14 days. The dried leaves were then pulverized with electric blender. Some weighed sample was macerated in 300 mL 70% methanol at room temperature for 72 hours with occasional shaking. The suspension was filtered with a white muslin cloth and filtrate was concentrated at 60°C with rotary evaporator. The resultant concentrate was oven-dried completely at 40°C to obtain the *Vernonia amygdalina* methanol leaf extract (VAM), which was then stored in the biofreezer at -4°C until when needed.

2.4. Experimental Animals

Twenty five healthy male albino wistar rats (137 – 223 g) were used in this study. They were obtained from the Animal House of the Department of Biological Sciences, College of Basic and Applied Sciences, Mountain Top University, Nigeria. The animals were kept in clean cages and were given food and water ad libitum. The room housing the animals was well ventilated with 12 h light/dark cycle and 65 ± 2% humidity, throughout the period of the experiment. The animals were handled in conformity with International, National and Institutional Guidelines for Care and Use of Laboratory Animals in Biomedical Research as declared by the Canadian Council of Animal Care [26].

2.5. Induction of Diabetes

Each of twenty adult male fasted rats were induced with single dose of 45 mg/kg body weight of streptozotocin (STZ) dissolved in citrate buffer (0.01 M, pH 4.5) by single intraperitoneal injection. After seventy-two hours of induction, the animals were fasted and 5% glucose solution was given to the animals for 12 hours in order to overcome the adverse effects of STZ-induced hypoglycemia. Thereafter, the blood glucose level was checked using glucometer (Accu-Chek® Active, Blood Glucose Monitoring System, Roche Diabetes Care, Inc. Indianapolis, USA). The animals with fasting blood glucose level ≥ 150 mg/dL were used for the study.

2.6. Distribution of Animals and Administration of Drug and VAM

Twenty-five male Wistar rats were used for the experiment. Five normal rats not diabetic induced with STZ served as control (received distilled water), while the twenty STZ-induced diabetic rats were distributed randomly and treated as follows: diabetic untreated group (STZ), diabetic + metformin (STZ + MET), diabetic + *V. amygdalina*, 150 mg/kg body weight (STZ + VAM 150 mg) and diabetic + *V. amygdalina*, 300 mg/kg body weight (STZ + VAM 300 mg). Metformin and extract were dissolved in distilled water and given by oral gavage for 7 days. Before the animals were sacrificed, they were fasted overnight and the fasting blood glucose (FBG) was measured with Accu Check glucometer.

2.7. Collection and Preparation of Blood Plasma, Liver and kidney Samples

The animals were sacrificed by cervical dislocation under 10% chloroform anaesthesia. Blood sample was collected through the ocular into well labelled heparin bottles. Blood sample was centrifuged at 2,500 x g for 10 minutes to obtain blood plasma used for determination of lipid profile. Livers and kidneys were also collected after dissection of rats into a beaker of water to remove blood and the water was blotted out with a piece of tissue paper. Their weights were determined and then homogenized with pestle and mortal in normal saline solution. The homogenates were centrifuged at 4,000 x g for 10 minutes to obtain the liver and kidney supernatants for enzymes and biochemical assays.

2.8. Estimation of Plasma Lipid Profile

Lipid profile of the plasma sample was estimated for total cholesterol (CHOL), triglyceride (TRIG), high density lipoprotein-cholesterol (HDL), low density lipoprotein-cholesterol (LDL) and very low density lipoprotein-cholesterol (VLDL) using standard laboratory kit from Randox laboratories, UK. Low Density Lipoprotein-cholesterol was estimated according to equation as shown below:

LDL-Cholesterol (mg/dl) = TC- HDL- (TG/5)

However, TG/5 is equals to the concentration of Very Low Density Lipoprotein-cholesterol, while TC = total cholesterol and TG = triacylglycerol [23, 27].

2.9. Estimation of Liver and Kidney Enzymes Activities and Biochemical Parameters

Liver and kidney enzymes activities and other biochemical parameters were estimated in the liver and kidney supernatants obtained. Aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyltranferase (GGT), lactate dehydrogenase (LDH), total protein (TPRO), creatinine (CREA) and total bilirubin (TBIL) were estimated using standard laboratory kit from Randox laboratories, UK.

2.10. Data Analysis

All data were expressed as mean ± standard error of mean (SEM). Statistical analysis was carried out using Statistical Package for Social Science (SPSS) version 20 by one-way analysis of variance using Tukey HSD to separate homogeneous groups. Values were considered to be significantly different at $p < 0.05$.

3. Results

3.1. Weight of Animals Weight of Organs and Organ: Animal Ratio in Diabetic and VAM Treated Rats

There was no significant change ($p>0.05$) in the weight of diabetic induced rats in day 4 compared with the normal control rats on day 1 while noticeable reduction of weight was recorded in rats treated with 300 mg/kg VAM on day 11, the final day of the experiment (Figure 1). Weight of liver in diabetic rats was not significantly (>0.05) reduced whereas the liver weights in metformin and VAM treated rats were significantly ($p<0.05$) reduced compared with the control rats (Figure 2). However, there was no significant difference in the weight of kidney in diabetic and treated rats compared with the control (Figure 2). There was slight reduction in liver/animal weight ratio in diabetic rats whereas the liver/animal weight ratios in rats treated with metformin and VAM reduced significantly ($p<0.05$) compared with the control rats but no significant difference ($p>0.05$) in the kidney/animal weight ratio in treated rats compared with the control (Figure 3).

Figure-1. Effect of VAM on average weight of streptozotocin-induced diabetic rats; Values represent mean, (n= 5); WGT-Weight, STZ-streptozotocin-induced diabetic rats; VAM-*V. amygdalina*

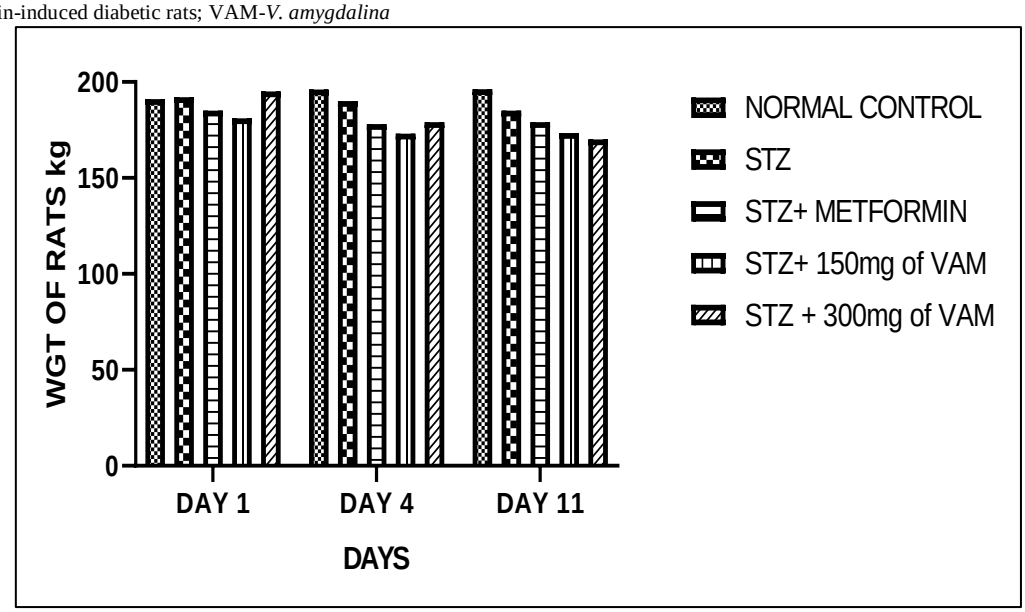


Figure-2. Effect of VAM on average of organs (liver and kidney) in streptozotocin (STZ)-induced diabetic rats. Values represent mean, (n=5). STZ-Streptozotocin-induced diabetic rats, MET-Metformin, VAM-*V. amygdalina*

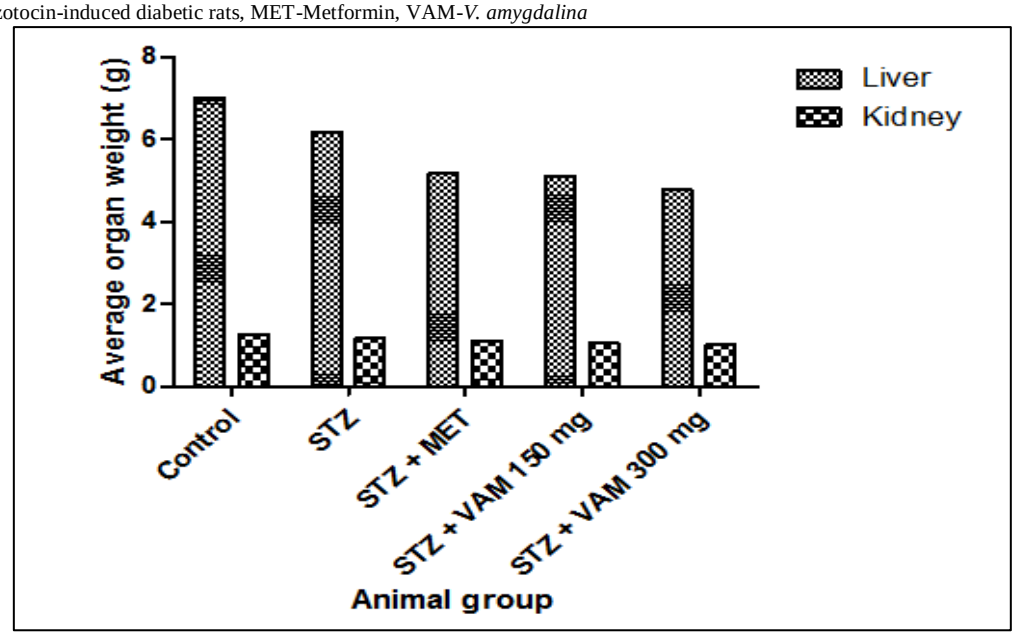
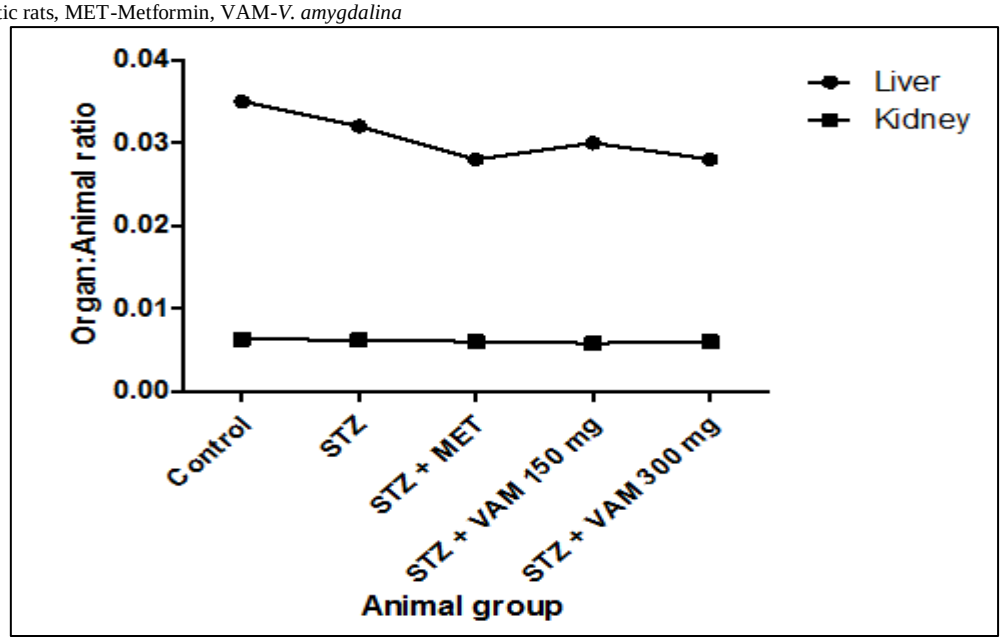


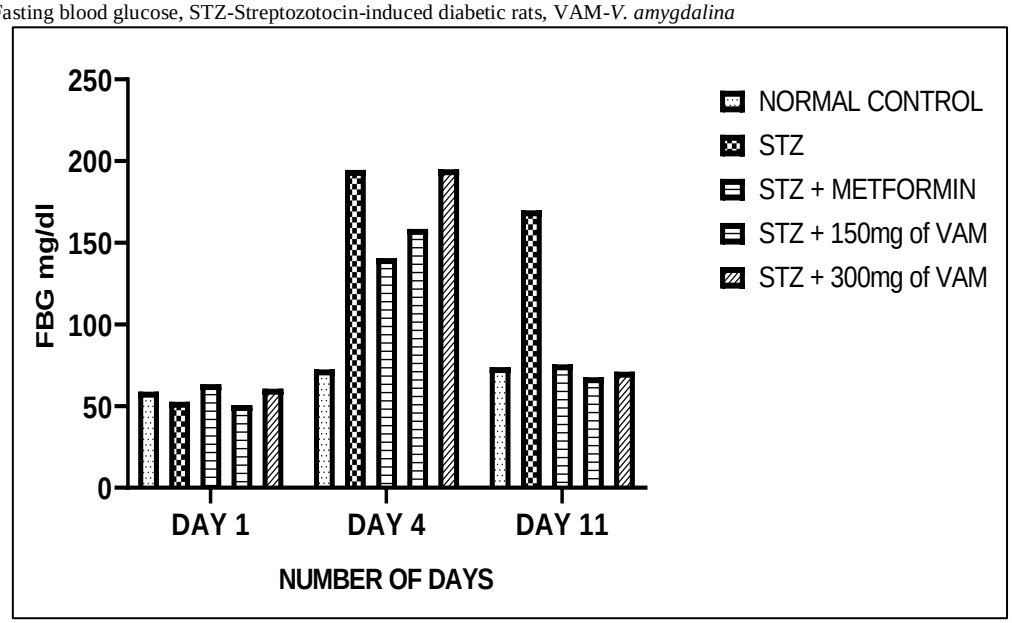
Figure-3. Effect of VAM on organ-animal ratio in streptozotocin (STZ)-induced diabetic rats. Values represent mean, (n=5); STZ-Streptozotocin-induced diabetic rats, MET-Metformin, VAM-*V. amygdalina*



3.2. Fasting Blood Glucose (FBG) Level in Diabetic and VAM Treated Rats

Induction of diabetes with streptozotocin significantly ($p<0.05$) elevated the FBG level on the 4th day compared with the control rats whereas treatment with metformin and VAM for 7 days (day 11) significantly ($p<0.05$) reduced the FBG level compared with diabetic (STZ) group and there was no significant ($p>0.05$) difference in FBG level of treated rats with the normal control (Figure 4).

Figure-4. Effect of VAM on concentration of fasting blood glucose (FBG) in streptozotocin (STZ)-induced diabetic rats; Values represent mean, (n=5); FBG-Fasting blood glucose, STZ-Streptozotocin-induced diabetic rats, VAM-*V. amygdalina*



3.3. Plasma Lipid Profile in Diabetic and VAM Treated Rats

There were significant ($p<0.05$) decrease in TRIG, HDL, LDL and VLDL concentrations and no significant ($p>0.05$) difference in CHOL concentration of diabetic induced rats compared with the control (Table 1). Whereas treatment with 150 mg/kg VAM and 300 mg/kg VAM reversed the effect, concentrations of CHOL, TRIG, HDL, LDL and VLDL were significantly ($p<0.05$) increased compared with the diabetic induced rats but significantly lower than the values of normal rats group except VLDL (Table 1). Likewise, metformin gave significant ($p<0.05$) increase in TRIG, LDL and VLDL concentrations but reduced HDL concentration compared with diabetic induced rats (Table 1).

Table-1. Effect of VAM on plasma lipid profile of streptozotocin-induced rats

Parameters (mg/dL)	NC	STZ	STZ+MET	STZ+150mg of VAM	STZ+300mg of VAM
CHOL	44.58±4.13	46.25±4.96	40.53±11.19	53.54±6.36^{a,}	49.0±5.45^{a}
TRIG	94.6±16.29	57.37±23.02^{a}	91.75±3.86^{b}	119.3±15.64^{a,b}	94.6±16.29^{b}
HDL	164.1±39.70	85.35±34.15^{a}	94.58±8.08^{a,b}	110.9±24.87^{a,b}	109.1±11.34^{a,b}
LDL	138.7±37.43	50.58±34.42^{a}	72.45±6.04^{a,b}	81.52±22.61^{a,b}	82.16±9.12^{a,b}
VLDL	19.06±3.26	11.47±4.59^{a}	18.4±0.80^{b}	24.12±3.19^{a,b}	22.02±2.27^{b}

Values expressed as mean ± SEM, (n=5). ^{a} is significant in comparison with normal control ($p<0.05$), ^{b} is significant in comparison with diabetic rats (STZ) ($p<0.05$). NC-Normal Control, STZ-Streptozotocin-induced diabetic rats, VAM-*V. amygdalina* extract, CHOL-Choletserol, TRIG-Triglyceride, HDL-High density lipoprotein-cholesterol, LDL-Low density lipoprotein-cholesterol, VLDL-Very low density lipoprotein-cholesterol.

3.4. Liver and Kidney Enzymes Activities

AST activity in the liver of rats treated with metformin and doses of VAM were significantly ($p<0.05$) decreased whereas VAM significantly elevated AST activity in the kidney compared with diabetic and control rats (Figure 5). At 150 mg/kg VAM, the liver and kidney ALT activities were significantly ($p<0.05$) increased compared with diabetic and control rats (Figure 6). MET and VAM significantly ($p<0.05$) increased GGT activity in the liver whereas MET and VAM significantly decrease the enzyme activity in the kidney compared with diabetic and control rats (Figure 7). Doses of VAM significantly ($p<0.05$) increased the activity of LDH in the liver while it reduced the activity in the kidney (Figure 8). The TPRO concentration, though higher in the liver, was significantly ($p<0.05$) reduced in rats treated with MET and VAM compared with diabetic and control rats whereas there was no significant ($p>0.05$) change in TPRO in the kidney (Figure 9). As MET significantly ($p<0.05$) increased CREA concentration, VAM reduced it in the liver compared with diabetic rats while it was significantly ($p<0.050$ increased in the kidney by MET and VAM compared with the control (Figure 10). The rats group treated with MET significantly ($p<0.05$) reduced TBIL concentration in the liver whereas, VAM treated rats significantly ($p<0.05$) reduced TBIL concentration in the kidney (Figure 11).

Figure-5. Effect of VAM on liver and kidney aspartate aminotransferase (AST) activities (U/L) in streptozotocin (STZ)-induced diabetic rats; Values represent mean ± SEM (standard error of mean), (n=5); STZ-Streptozotocin-induced diabetic rats, MET-Metformin, VAM-*V. amygdalina*

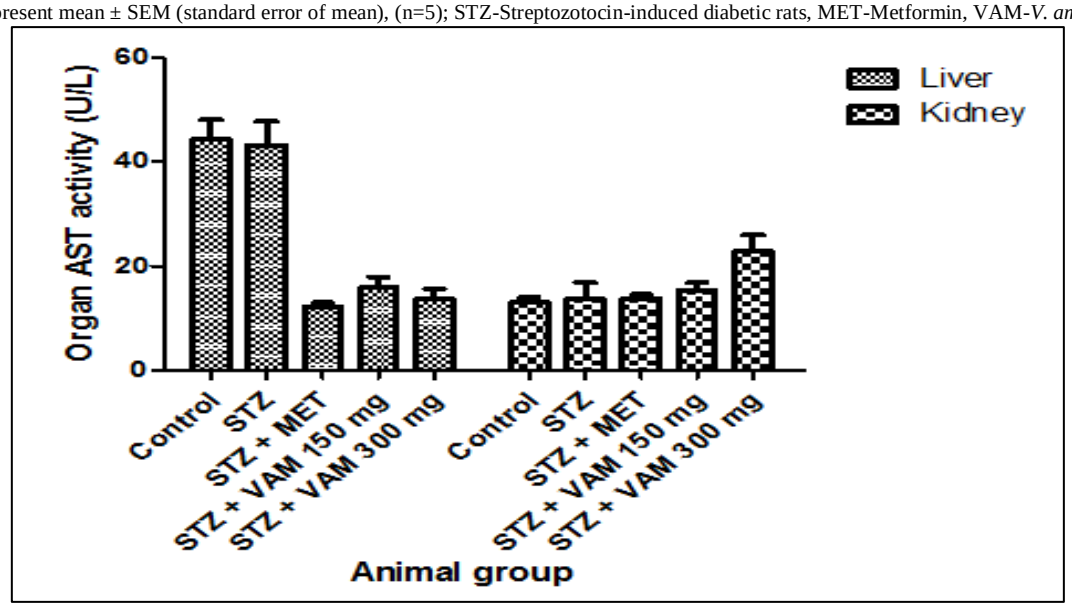


Figure-6. Effect of VAM on liver and kidney alanine aminotransferase (ALT) activities (U/L) in streptozotocin (STZ)-induced diabetic rats; Values represent mean ± SEM (standard error of mean), (n=5); STZ-Streptozotocin-induced diabetic rats, MET-Metformin, VAM-*V. amygdalina*

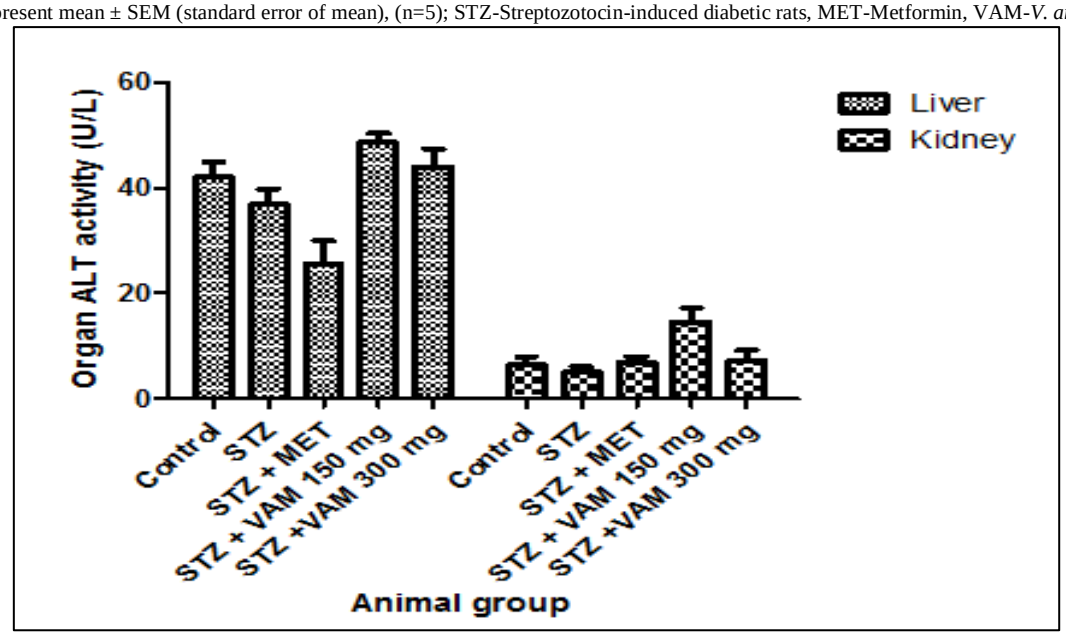


Figure-7. Effect of VAM on liver and kidney gamma-glutamyl transferase (GGT) activities (U/L) in streptozotocin (STZ)-induced diabetic rats; Values represent mean ± SEM (standard error of mean), (n=5); STZ-Streptozotocin-induced diabetic rats, MET-Metformin, VAM-*V. amygdalina*

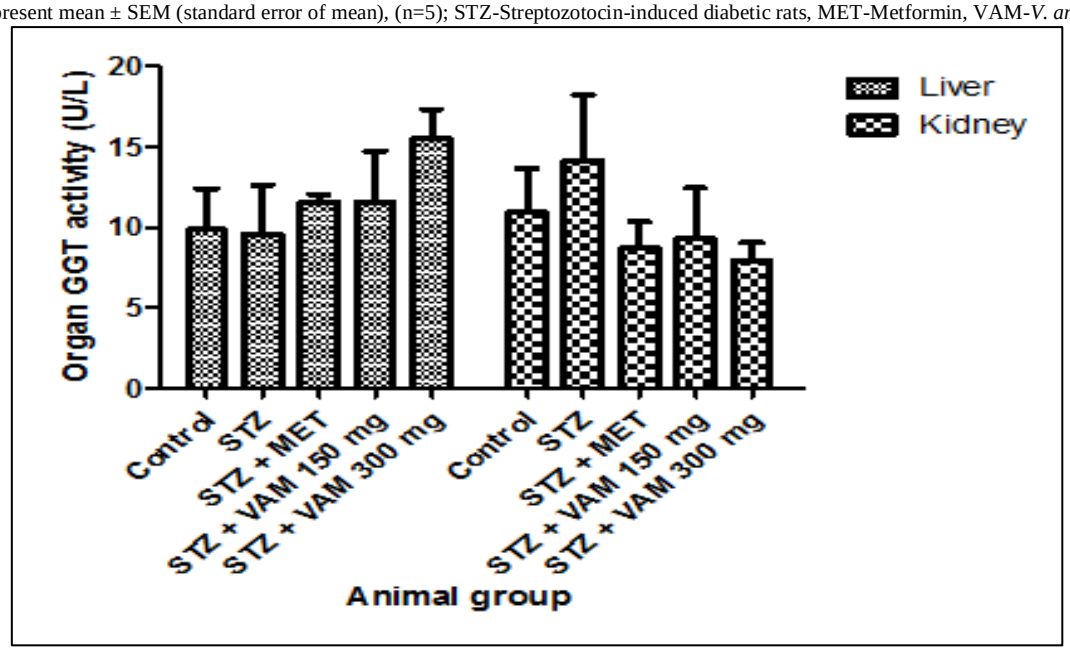


Figure-8. Effect of VAM on liver and kidney lactate dehydrogenase (LDH) activities (U/L) in streptozotocin (STZ)-induced diabetic rats; Values represent mean ± SEM (standard error of mean), (n=5); STZ-Streptozotocin-induced diabetic rats, MET-Metformin, VAM-*V. amygdalina*

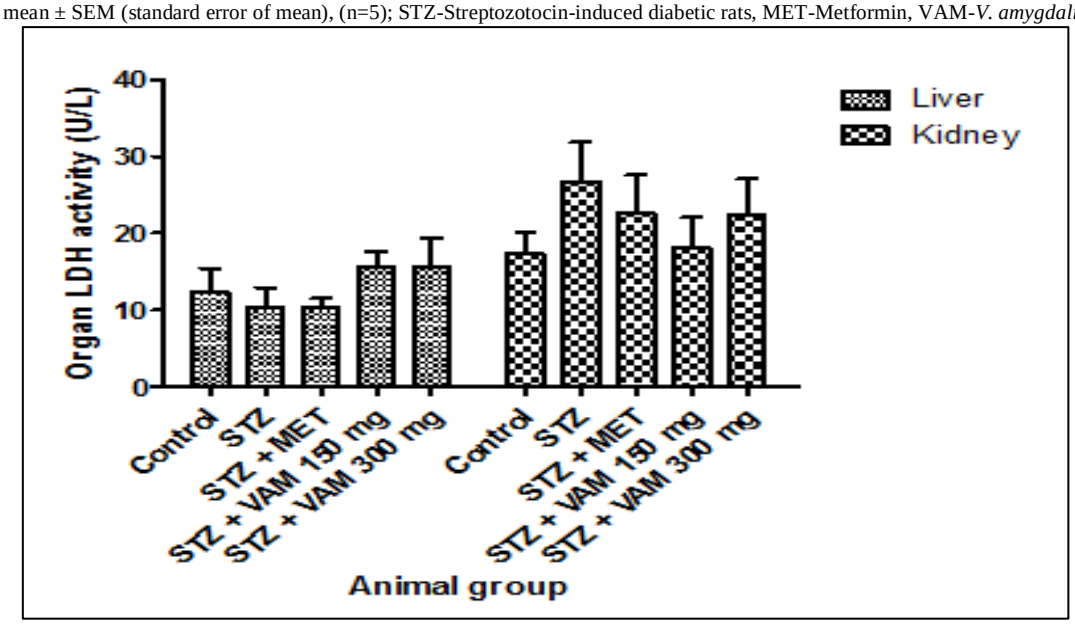


Figure-9. Effect of VAM on liver and kidney total protein (TPRO) concentrations (g/dL) in streptozotocin (STZ)-induced diabetic rats; Values represent mean ± SEM (standard error of mean), (n=5); STZ-Streptozotocin-induced diabetic rats, MET-Metformin, VAM-*V. amygdalina*

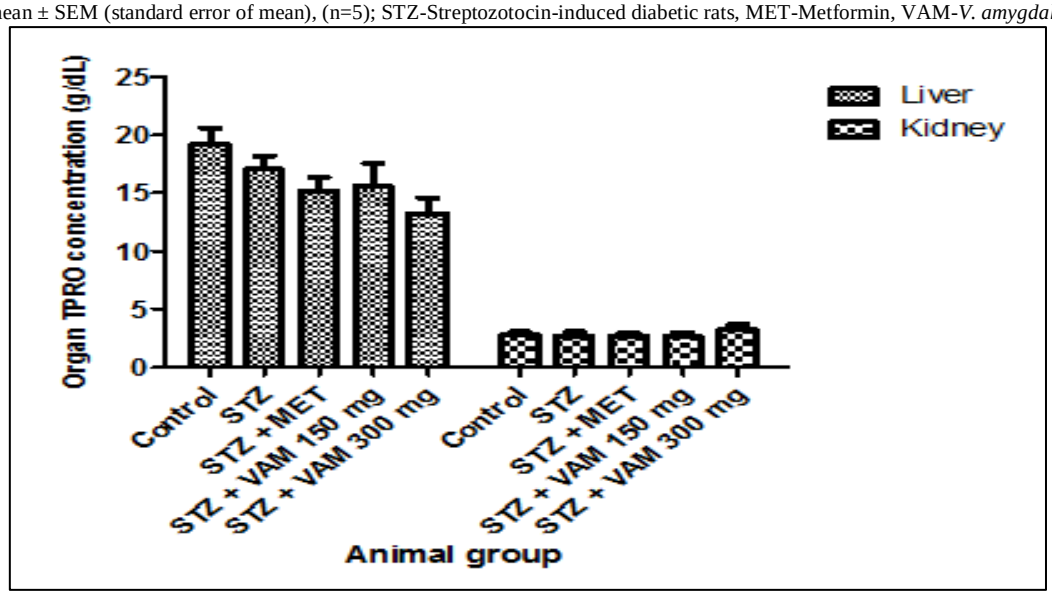


Figure-10. Effect of VAM on liver and kidney creatinine (CREA) concentrations (g/dL) in streptozotocin (STZ)-induced diabetic rats; Values represent mean ± SEM (standard error of mean), (n=5); STZ-Streptozotocin-induced diabetic rats, MET-Metformin, VAM-*V. amygdalina*

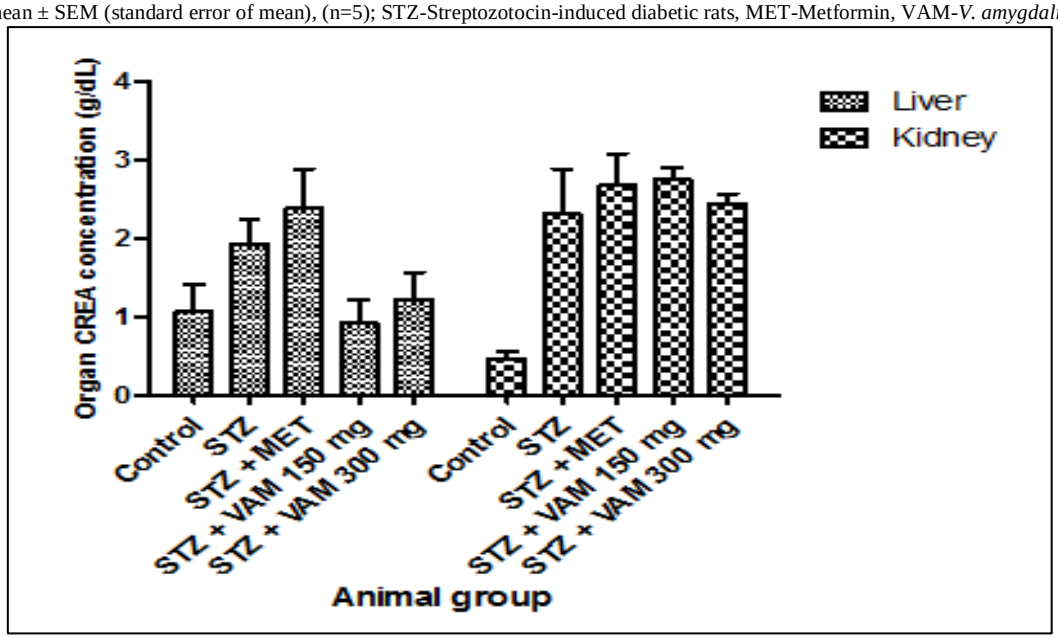
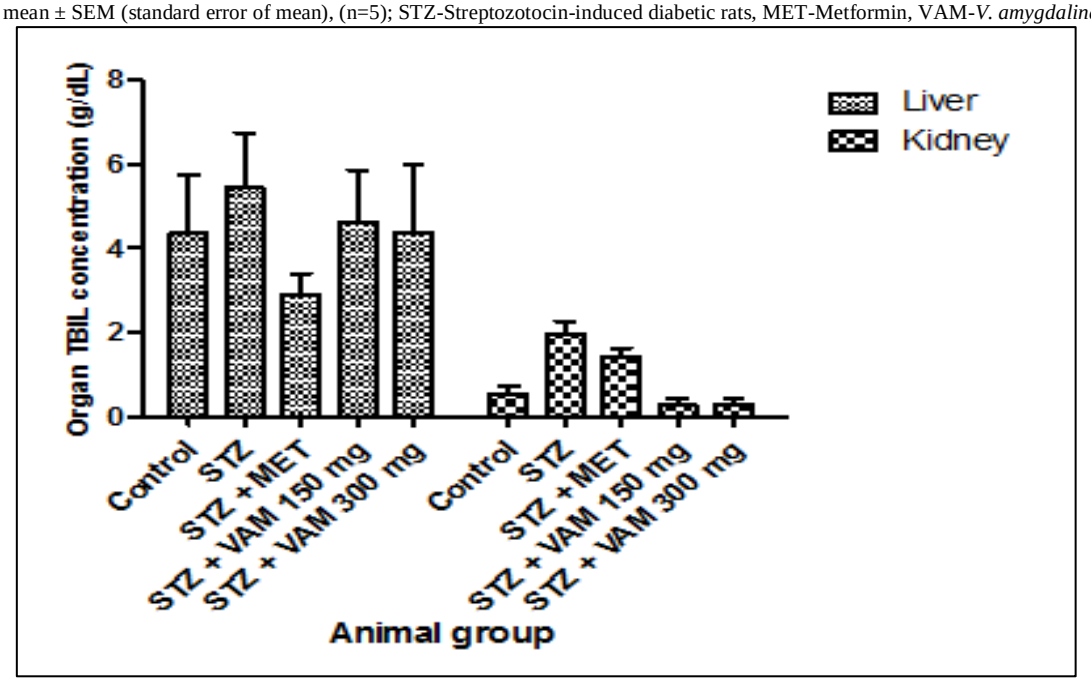


Figure-11. Effect of VAM on liver and kidney total bilirubin (TBIL) concentrations (g/dL) in streptozotocin (STZ)-induced diabetic rats; Values represent mean ± SEM (standard error of mean), (n=5); STZ-Streptozotocin-induced diabetic rats, MET-Metformin, VAM-*V. amygdalina*



4. Discussion

Diabetes is a chronic disease which is characterized by hyperglycemia with serious disturbances in the metabolism of carbohydrates, lipids and proteins [28, 29]. Significant increase of the fasting blood glucose (FBG) in diabetic-induced rats group compared with the normal control group suggest there is a disruption in the carbohydrate metabolism and streptozotocin is a common agent used to induce diabetes in rats which may explain the reason for the hyperglycemia noticed in the diabetes rats. Meanwhile, administration of metformin, a pharmaceutical drug used to treat diabetes and doses of VAM significantly reduced the level of FBG compared with the diabetes rats but there was no significant difference with the normal control group suggests the antihyperglycemic potential of VAM.

Changes in the body weight of animals generally indicate the status of its health [30]. There was no significant difference in weights of animal, liver, kidney and organ/animal ratios in different groups of treated animals compared with normal control group. This shows that VAM has no negative impact on the animal, liver and kidney which may suggest its safety and reason for its consumption as vegetable soup and herbal medication.

Dyslipidemia in diabetes is characterized by elevated levels of TRIG, LDL, CHOL and low level of HDL. Many studies have also reported the impaired lipoprotein lipase (LPL) action in diabetic dyslipidemia, and the negative role played by LDL to induce vascular and renal cellular dysfunction and cardiovascular risk in diabetic complications [31-33]. However, a study by Ugwu, *et al.* [34] showed a contrary results where there were low levels of total CHOL, TRIG and LDL in diabetic patients [34]. Likewise in this study, administration of diabetic inducing agent, streptozotocin significantly reduced the levels of TRIG, HDL, LDL and VLDL compared to the control group which could be due to lipolysis as a result of the activity of lipase enzyme by hydrolyzing primarily TRIG and other lipid components to fatty acids and glycerol in the diabetic animals. Whereas in the VAM treated animal groups, there was a reversal of these lipid parameters that is, TRIG, HDL, LDL and VLDL levels were significantly elevated compare with the diabetic animal group and normal control which may suggest that VAM could have induced lipogenesis by increasing the activity of fat synthesizing enzymes such as fatty acid synthase.

Liver enzymes alanine aminotransferase (ALT) and gamma glutamyl transferase (GGT) are markers for type 2 diabetes mellitus (T2DM) [6]. Generally, liver enzymes measurement which are accessible, are now widely used for detecting the incidence, development, and prognosis of liver disease with obvious clinical symptoms, assessing overall health status and liver metabolic status [35, 36]. GGT is used to predict occurrence of future diabetes whereas, ALT is known to increase with insulin resistance, a predictor of T2DM and the most specific marker of hepatic pathology [37, 38]. Although, some studies have reported a strong relationship between GGT and diabetes than between ALT and diabetes, others reported the opposite [39-41]. This study showed non-significant reduction in the activities of liver AST, ALT, GGT and LDH in induced diabetic group compared with normal control group while there was significant increase in activities of the liver ALT, GGT and LDH, and reduced activity of AST in the VAM treated groups compared with the diabetic group. Organs such as liver, kidney, heart and pancreas have abundant of these enzymes. However, any injury to the organs will release the enzymes into the blood stream where it could be used for diagnosis. Elevation of these enzymes in the liver may be due to the ability of the organ to respond to enzyme synthesis and may not be as a result of liver damage. The kidney level of AST and ALT slightly increased whereas GGT and LDH groups were reduced in VAM treated rats compared to the diabetic group. There was reduction in the TPRO, CREA and TBIL in the liver of VAM treated groups while these parameters were increased in the kidney except TBIL. However, AST, ALT, TPRO and TBIL were higher in liver than kidney while LDH and CREA were higher in the kidney.

5. Conclusion

In conclusion, this study has revealed the modulatory role of VAM on diabetes induced dyslipidemia, and liver and kidney enzymes in diabetic rats. It has shown the potential of VAM to increase the activities of ALT, GGT and LDH while reducing AST in the liver. Furthermore, VAM reduced the concentrations of TPRO, CREA and TBIL in the liver whereas these parameters were increased in the kidney. Finally, VAM increased the levels of AST, ALT, TPRO and TBIL in the liver than in the kidney while LDH and CREA were increased in kidney than the liver. This suggest that the plant should be taken with caution.

Ethical APPROVAL

This study was approved by the Research and Ethics Committee of the College of Basic and Applied Sciences, Mountain Top University, Nigeria.

Conflict of Interest

There is no conflict of interest in this research work

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