



# Hypoglycaemic and Hypolipidemic Properties of Ethyl Acetate Fraction of *P. americana* Leaf in Alloxan-Induced Diabetic Rats

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**Abstract:** Diabetes is a heterogeneous disorder with multiple etiologies resulting in major healthcare problem such as risk of heart disease, stroke and micro-vascular complications such as blindness, renal failure and peripheral neuropathy. The research was aimed at evaluating the antihyperglycaemic and antihyperlipidemic potentials of ethyl acetate fraction of *Persea americana* leaf in alloxan-induced diabetic rats. *Persea americana* leaf was extracted by soxhlet extraction for 24hrs and concentrated in vacuo to yield *Persea americana* extract (PAE). Elemental compositional analysis of the extract was determined using flame atomic absorption spectroscopy. Hyperglycemia was induced by intraperitoneal administration of alloxan. Blood glucose levels determined using ACCUCHEK. Hypoglycemic activity was evaluated by measuring serum glucose level and insulin level. Hypolipidemic activity was evaluated by measuring various biochemical parameters like total cholesterol, triglycerides, low density lipoprotein, very low density lipoprotein and high density lipoprotein. Elemental compositional analysis of the Fraction reveals the presence of Zn, Cr, Mg, Fe, Cu and Mn. The levels of fasting blood glucose were found to decrease significantly in the treated groups in a dose dependent pattern with reversal in body weight lost as well as significant increase in serum insulin level compared with the diabetic control group. The results showed that serum total cholesterol, triglyceride, low density lipoprotein and very low density lipoprotein levels were statistically lower in the treated groups. The observed hypoglycaemic alongside with hypolipidemic effect can be associated with the levels of trace elements present in the extract. The present study support the traditional claim in the use of ethyl acetate extract of *P. americana* leaf as hypoglycaemic and hypolipidemic agent.

**Keywords:** Diabetes, Hypolipidemia, *Persea americana*, Alloxan, Lipid Profile, Fasting Blood Glucose

## 1. Introduction

Diabetes mellitus defined as a syndrome characterized by persistent hyperglycaemia associated with disturbance in carbohydrate, protein and lipid metabolism as a result of absolute or relative deficiency in insulin secretion or action as well as increased cellular resistance to that hormone with dysfunction in organ systems. The increasing incidence of the disease worldwide may be due to sedentary life style,

unhealthy diet, obesity and other predisposing risk factors [1, 2]. Complications of diabetes mellitus include hypertension, atherosclerosis and microcirculatory disorder [3], retinopathy, nephropathy, and foot ulceration [4]. It is projected by 2040 to become of the world's main disablers and killers, as the number of people with diabetes multiplies worldwide [5]. The World Health Organization has also recommended the evaluation of the effective use of plants, because the use of modern drugs is not safe [6] [7], with 70-

80% of people worldwide use herb for management of mild to moderate illnesses [8-10]. The synthetic hypoglycemic agents used in clinical practices have serious side effects like haematological effects, coma, disturbances of liver and kidney [11, 12, 13]. Many medicinal plants used in ethnomedical practices in Nigeria are known or little known to scientific world. *P. americana*, is originated in the state of Puebla, Mexico. The native, undomesticated variety is known as a criollo, and is small, with dark black skin, and contains a large seed [14]. One of the most fascinating areas of avocado research and one that may turn out to be the most unique for health support involves carbohydrates and blood sugar regulation [15] and may play an important role in the development of nutraceuticals [16]. The main objective of the study was to assess the hypoglycaemic and hypolipidemic potential of leaves.

## 2. Materials and Methods

### 2.1. Sample Collection and Identification

The leaf of *Persea americana* were collected from Jos, Plateau state of Nigeria. The plant part was authenticated by a Botanist at Plant Science Department, B. U. K. with accession number BUKHAN 0305 and was deposited in Bayero University, Kano herbarium for reference.

### 2.2. Extraction of Plant Material

Soxhlet extraction method was used for the extraction of the plant materials. The sample was chopped into small pieces and then shades dried and ground into powdered form. Ethyl acetate was used as the extraction solvent and later concentrated in vacuo using rotary evaporator at 40°C.

### 2.3. Elemental Composition Determination

Elemental compositional analysis of ethyl acetate fraction of *P. americana* leaf was carried out using flame atomic absorption spectroscopy [17].

### 2.4. Experimental Animals

Experimental rats (80-100g) of either sex were obtained from the Physiology department, Faculty of Basic Medical Sciences, Bayero University, Kano were used for the experiments. The animals were kept in cages and clean drinking water provided *ad libitum* while they were fed with standard commercial pelleted feed (Vital Feed® Nigeria). The temperatures varied between 27-30°C and relative humidity of about 55%-60% with 12-h light-dark cycle and adequate ventilation maintained in the animal house. Ethical conditions governing the conducts of experiments with life animals as stipulated were strictly observed. Also, the experimental protocol was approved by the College of Health Science ethical committee.

### 2.5. Experiment Design

A total of 30 albino rats were used for this experiment and

they were divided into six groups of 5 rats each.

Group 1- normal rats

Group 2- diabetic control rats.

Group 3- diabetic rats treated with ethyl acetate *P. americana* leaf (100mg/kg)

Group 4- diabetic rats treated with ethyl acetate *P. americana* leaf (200mg/kg)

Group 5- diabetic rats treated with ethyl acetate *P. americana* leaf (400mg/kg)

Group 6- diabetic rats treated with glucophage (84mg/kg).

The studies lasted for a period of four weeks. The level of fasting blood glucose was determined weekly by tail tipping. At the end of 4 weeks treatment, the rats were sacrificed and blood samples collected for insulin level and lipid profile (total cholesterol, triglyceride, high density lipoproteins, low density lipoproteins and very low density lipoproteins) determination. Histopathological analysis of the pancreas was also carried out.

### 2.6. Experimental Induction of Diabetes

Alloxan induction was conducted according to the works of [18, 19, 20]. Diabetes was induced by single intraperitoneal injection of alloxan monohydrate (100mg/kg). After 48hrs of induction, rats with 180mg/dl and above fasting blood glucose were chosen for the study [21]. As alloxan is capable of producing fatal hypoglycaemia as a result of massive pancreatic insulin release, rats were being fed with 20% glucose e solution in order to prevent severe hypoglycaemia [22].

### 2.7. Fasting Blood Glucose Determination

Fasting blood glucose (FBG) levels were determined with the aid of ACCU-CHEK Advantage II Active glucometer and strips. The test strip was inserted into the glucometer; blood sample was collected from the tail of the rat by tail tipping using a surgical blade. The blood was dropped on the dextrostix reagent pad. This was inserted into microprocessor digital blood glucometer and the readings were recorded [23] in mg/dl. Insulin was determine according to the method of [24, 25].

### 2.8. Hypolipidemic Assay

Hypolipidemic activity of the extract was evaluation after 4 weeks of extract administration the rats were anaesthetized with chloroform vapour and the blood was collected through cardiac puncture into sample bottles devoid of anticoagulant. The samples were centrifuged at 1000 rpm for 15 mins to obtain the sera. Serum total cholesterol, triglyceride and high density lipoprotein (HDL) levels were measured by enzymatic colorimetric methods using Randox diagnostic kits. The concentrations of low density lipoprotein (LDL) and very low density lipoprotein (VLDL) were calculated from the formula of [26].

### 2.9. Statistical Analysis

Data are presented as mean  $\pm$  SEM and were analyzed

statistically using One way ANOVA followed by Tukey-kramer multiple comparison test and values with  $P < 0.05$  were considered significant.

### 3. Results

#### 3.1. Elemental Compositional Analysis of Ethyl Acetate Fraction *P. americana* Leaf

A total of 8 elements were analyzed. The most abundant elements were Fe, Mg, Zn and Cr with mean concentrations exceeding  $100\mu\text{g/g}$  (Table 1).

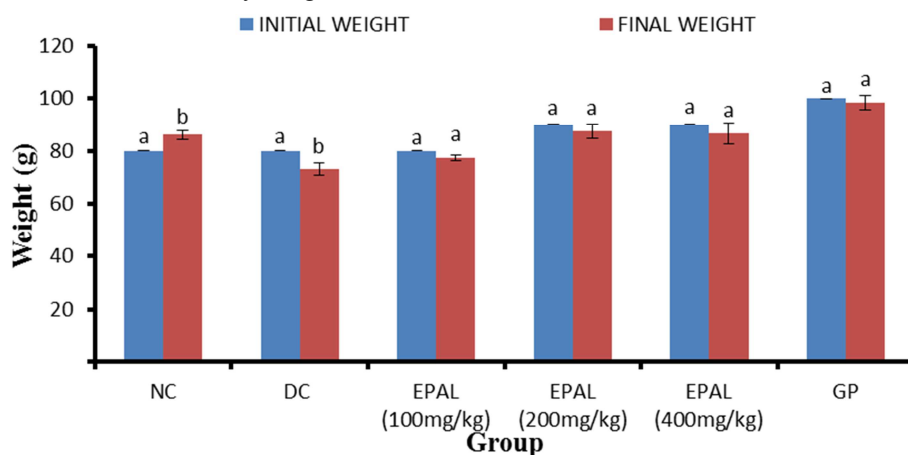
#### 3.2. Effect of Ethyl Acetate Fraction *P. americana* Leaf on Alloxan-induced Diabetic Rats

There were observable changes in the body weight of treated and untreated alloxan-induced diabetic rats. Significant decrease in body weight was observed in diabetic control group, whereas an increase in body weight was seen

in the treated groups (Figure 1). Administration of ethyl acetate fraction of *P. americana* produced a significant reduction ( $P < 0.05$ ) in fasting blood glucose level in alloxan-induced diabetic rats treated with the fraction. These effect were statistically significant ( $P < 0.05$ ) from week one and progressed to week 4 (Figure 2). The serum insulin levels of alloxan-induced diabetic treated with ethyl acetate fraction of *P. americana* was found to increase significantly when compared with diabetic control group (Figure 3).

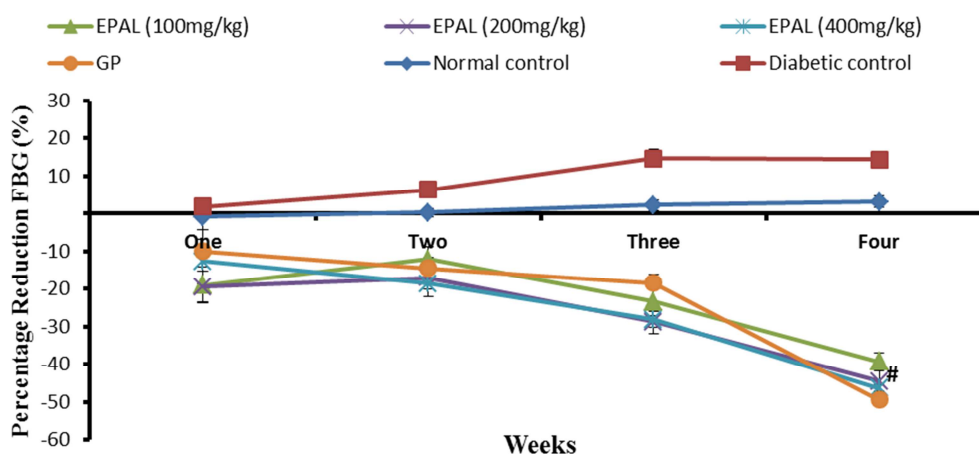
#### 3.3. Effect of Ethyl Acetate Fraction of *P. americana* Leaf on Lipid Profile of Alloxan - Induced Diabetic Rats

Administration of ethyl acetate fraction of *P. americana* leaf caused significant decrease ( $P < 0.05$ ) in the levels of serum total cholesterol, triglycerides, LDL and VLDL of alloxan-induced diabetic treated rats. However, HDL levels of the treated rats as well as diabetic control group were not significantly affected (Figure 4).



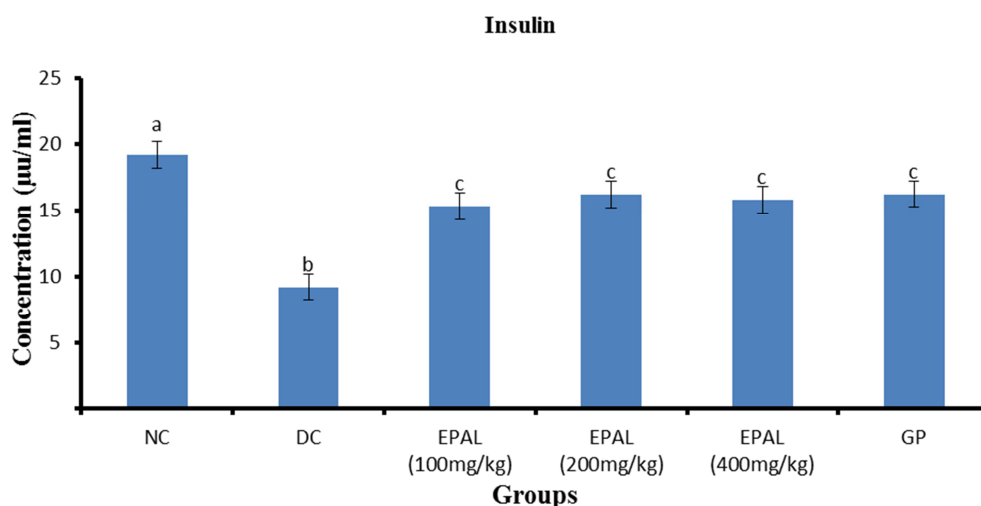
**Figure 1.** Initial and Final Body Weights of Alloxan Induced Diabetic Rats Administered with EPAL Leaf (100, 200 and 400mg/kg b.w.) and Glucophage (84mg/kg b.w.) For 4 Weeks.

Results are presented as Mean  $\pm$  SD (n=5). Values with the different superscripts are significantly different ( $P < 0.05$ ), NC= Normal control, DC= Diabetic control, GP= Glucophage, EPAL=Ethyl acetate extract of *P. americana* leaf



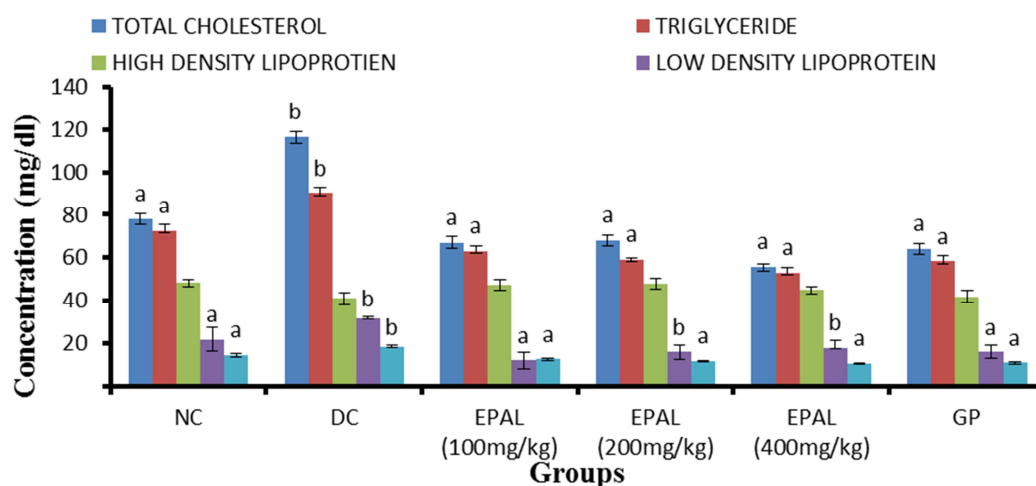
**Figure 2.** Percentage Reduction of FBG of Alloxan-Induced Diabetic Rats Administered with EPAL (100, 200 and 400mg/kg b.w.) and Glucophage (84mg/kg b.w.) For 4 Weeks.

Results are presented as Mean  $\pm$  SD (n=5). '#' indicates significant difference ( $P < 0.05$ ) with reference to diabetic control, EPAL= ethyl acetate extract of *P. americana*, GP= glucophage



**Figure 3.** Insulin Levels of Alloxan-Induced Diabetic Rats Administered with EPAL (100, 200 and 400mg/Kg b.w.) and Glucophage (84mg/Kg b.w.) For 4 Weeks.

Results are presented as Mean  $\pm$  SD (n=5). Values with different superscripts are significantly different ( $P < 0.05$ ) with respect to normal control, NC=normal control, DC=diabetic control, EPAL=ethyl acetate extract of *P. americana* leaf



**Figure 4.** Serum Levels of TC, TAG, HDL, LDL and VLDL of Alloxan-Induced Diabetic Rats Administered with EPAL (100, 200 and 400mg/kg b.w.) and Glucophage (84mg/kg b.w.) For 4 Weeks.

Results are presented as Mean  $\pm$  SD, n=5. Values with the different superscripts are significantly different ( $P < 0.05$ ) with respect to normal control, NC= Normal control, DC= Diabetic control, GP= Glucophage, EPAL=Ethyl acetate extract of *P. americana* leaf

**Table 1.** Elemental Compositional Analysis of Ethyl acetate Fraction *P. americana* Leaf.

Elements	Concentration (µg/g)
Fe	406.2 $\pm$ 1.07 <sup>a</sup>
Mn	42.6 $\pm$ 0.92 <sup>b</sup>
Mg	573.8 $\pm$ 0.12 <sup>c</sup>
Ni	1.02 $\pm$ 0.03 <sup>d</sup>
Zn	110.6 $\pm$ 0.07 <sup>e</sup>
Cu	2.71 $\pm$ 0.32 <sup>f</sup>
Mo	2.54 $\pm$ 0.04 <sup>g</sup>
Cr	130.7 $\pm$ 0.96 <sup>h</sup>

Results are presented as Mean  $\pm$  SD (n=3). Values bearing different superscripts are significantly different ( $P < 0.05$ )

## 4. Discussion

Diabetes mellitus causes a drastic change in body weight

[27, 28], which may be due to excessive breakdown of tissue proteins and lipids caused by insulin insufficiency. Evaluation of hypoglycemic and hypolipidemic activities of ethyl acetate fraction of *P. americana* leaf were carried out in alloxan-induced diabetic rats. The extract was observed to demonstrate significant antidiabetic [28] and hypolipidemic activities in alloxan-induced diabetic rats. The observed hypoglycemic activity might be associated with the presence of some trace element in the extract such as Zn, Cr, Mg, Mn etc. Zinc was shown to play important roles in synthesis, storage and secretion of insulin as well as conformational integrity of insulin i.e Zn-insulin complex [29, 30]. Chromium (glucose tolerance complex) and magnesium (act as metal-enzyme complex in activation of enzymes like hexokinase, phosphofructokinase and fructokinase) might also contribute to the observed hypoglycemic effect. There

are a lot of reports implicating some elements in plants as being responsible for their antidiabetic activities [31, 32, 33]. These constituents may in part be responsible for the observed significant activity of this extract either singly or in synergy with one another [34]. Alloxan is reported to selectively destroy insulin secretory beta-cells to impair insulin secretion and function [35, 36]. Decreased plasma insulin in hyperglycemic conditions increases fatty acyl coenzyme A oxidase activity, which initiate  $\beta$ -oxidation of fatty acids, resulting in lipid peroxidation [37]. Increased insulin level observed in treated rats might be due to radical scavenging activities of antioxidants (fenton reaction) present in extract, as they are known to stimulate insulin secretion. According to [38] the hypoglycaemic property of plants can be attributed to the presence of trace element in the leaf of plant in addition to the facts that the pancreas shows rapid uptake and turnover rate of retained zinc. This was followed by a significant increase in body weight of the treated rats. This is a reverse to diabetic state characterised by a severe loss in body weight due to loss or degradation of structural proteins [39]. Muscle wasting, negative nitrogen balance and accelerated gluconeogenesis are among the hallmarks of uncontrolled diabetes [40]. Some plants' extracts are reported to exert hypoglycemic action by potentiating the insulin effect, either by stimulating the pancreatic secretion of insulin from the cells of islets of langerhans [41] or its release from bound insulin [42]. Serum lipids are known to be elevated during severe diabetes and have been implicated in the development of arteriosclerosis [43, 36]. Diabetes-induced hyperlipidemia is attributable to excess mobilization of fat from the adipose due to the under utilization of glucose [44]. According to studies by [45, 46, 47] it was shown that chronic insulin deficiency as observed in alloxan-induced hyperglycaemia in experimental animals is associated with diminished levels of LDL receptors, blood cholesterol and triglyceride [48, 49]. This results to an increase in LDL particles and consequently increases serum level of LDL. The significantly lowered cholesterol level may have attributed to the observed high HDL in the treated rats. The regression of the diabetic state due to the administration of the root extract may have increased the utilization of glucose, thereby depressing the mobilization of fat from peripheral fat depots, since insulin inhibits the hormone sensitive lipase, insulin deficiency or insulin resistance may be responsible for dislipidimia [50]. Mineral elements like Zn, Mg, Cr and Fe present in this extract have been reported to exert antilipidemic activity [51]. These may in part be responsible for both the antidiabetic and hypolipidemic activities of the leaf extract. In conclusion, the results of this present study show that *P. americana* leaf possessed antidiabetic and hypolipidemic properties. This confirmation justifies its use in traditional medicine for the treatment of diabetes and its complication.

## 5. Conclusion

This study indicated that *P. americana* leaf extract have

potentials to decrease blood glucose level as well as improving hyperlipidaemia. The observed effects can be associated with the levels of trace elements such as zinc, chromium and manganese present in the extract. The present study, also supported the traditional claim in the use of *P. americana* leaf as hypoglycaemic and hypolipidemic medicinal plant. Hence, the plant can be recommended in the management of diabetes and cardiovascular diseases after extensive molecular and toxicological studies.

## Conflict of Interest Statement

All authors do not have any possible conflicts of interest.

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