

# Alleviation of Diabetic Dyslipidemia in Alloxan-Induced Diabetic Rats using Aqueous Seed Extract of *Persea Americana*

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## ABSTRACT

Diabetes Mellitus is accompanied by hypercholesterolemia, hyperlipidemia and hepatic steatosis apart from hyperglycemia. Alleviation of diabetic dyslipidemia in alloxan-induced diabetic rats using aqueous seed extract of *Persea americana* on induced Albino rats. A total of thirty Albino rats were divided into six groups of 5 rats: Group A: normal control, Group B: Negative control, Group C: Positive control 1, Group D: positive control 2, Group E: Test group 1, Group F: Test group 2. Intoxication of albino rats with alloxan monohydrate produced low high density lipoprotein (HDL), increased triglycerides (TG), total cholesterol (TC) and low density lipoprotein (LDL) after hyperglycemia. Results obtained from the diabetic study showed that plant extracts decreased blood glucose in a dose dependent fashion. The decrease was significant when compared to positive control 1. Similarly, treatment with the seed extracts normalized the lipoprotein abnormalities in dose dependent manner. The positive control 2 using atorvastatin was effective in TG and TC reduction while High dose aqueous seed extract of *Persea americana* was effective in the normalization of LDL and HDL. Phytochemical composition of the aqueous seed extract gave reactions for alkaloids, flavonoids, tannins, saponins, phenols, steroids and cyanogenic glycosides. The findings may support acclaimed traditional use of *Persea americana* seed in controlling hyperglycemia in diabetes and its complications.

**Keywords:** *Persea Americana*, Phytochemicals, Antidiabetic, Antihyperlipidemia activities.

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### Highlights of this paper

- This study showed that *Persea americana* seeds have the valuable potentials for complementary therapy for the treatment of diabetes mellitus and its complications.
- The findings may support acclaimed traditional use of avocado pear seeds for controlling hyperglycemia in diabetes and its complications.

## 1. INTRODUCTION

Diabetes mellitus (DM) describes a metabolic disorder of multiple aetiology characterized by chronic hyperglycemia with disturbance of carbohydrate, fat and protein metabolism. Type 1 DM occurs when pancreas cannot produce insulin as a result of autoimmune disease characterized by T-cell mediated destruction of the beta cells while in Type 2 DM the pancreas cannot produce enough insulin for effective uptake of glucose to the target cell [1, 2]. Defects in insulin action and hyperglycemia could lead to changes in plasma lipoproteins in patients with diabetes. Most especially, in the case of type 2 diabetes, the obesity/insulin-resistant metabolic disarray that is at the root of this form of diabetes could itself lead to lipid abnormalities exclusive hyperglycemia [3]. Alternatively, diabetes mellitus is accompanied by hypercholesterolemia, hyperlipidemia and hepatic steatosis [4].

The hypercholesterolemia may be in part, a consequence of accelerated fatty acid oxidation, and/or de novo hepatic biosynthetic release of VLDL-C as well as the release of stored fatty acids from adipocytes without a corresponding increase in the rate of clearance from the blood by the lipoprotein lipase [5]. This unhealthy levels of the three main types of lipid/lipoprotein; HDL, LDL and triglycerides are associated with insulin daycation directly or indirectly [6]. There are two reasons to specifically correct lipoprotein abnormalities in patients with diabetes. These are to prevent pancreatitis due to severe hypertriglyceridemia and to reduce the risk of macrovascular complication via dyslipidemia [7]. The American Diabetes Association has published clinical goals for lipoprotein levels in adults with diabetes as follows; Optimal LDL cholesterol levels less than 100mg/dl(2.60mmol/L), Optimal HDL cholesterol levels more than 45mg/dl (1.15mmol/L), and desirable triglyceride levels less than 200mg/dl (2.3mmol/L) [8, 9]. The rationale for the LDL recommendation is based on the observations that adult patients with diabetes and no over macrovascular disease appear to have the same risk of development of cardiac arrest as nondiabetics who already have had cardiac arrest according to some recent literature reviews [8, 10].

Subsequently, the use of lipid-lowering medications in diabetic patients. Drug management of Diabetes mellitus without associated troublesome effect has also remained a challenge for conventional medical practice. This has necessitated exploration and screening of medicinal plants with acclaimed therapeutic efficacies in DM management as recommended by the WHO expert committee on DM [4, 11]. There are many herbal remedies suggested for diabetes and its complications. However, insufficient research has been done to access the purposeful benefits of *Persea americana* seeds. Its fruit juice is used for detoxification of blood and to balance blood sugar levels. Reducing the blood sugar level and normalizing dyslipidemia can have a huge impact on the patients' ability to prevent further complication e.g. hypertension [2].

*Persea americana* of the family, Lauraceae, is a native fruit of Mexico and Central America. The fruit is commonly referred to as Avocado pear, Alligator or Butter fruit. Reports have shown that fruits and leaves of *Persea americana* to be very useful in the treatment and management of various diseases [12]. The studies also provided further insight into the restorative and antioxidants activities of *Persea americana*. The pharmacological effects may be due to certain mineral elements and phytochemical compounds [2].

Therefore, the objective of this work is to investigate the therapeutic effects of the seed extracts of *Persea americana* on diabetes mellitus and lipid abnormalities on laboratory induced albino rats using synthetic drugs as control models.

## 2. MATERIALS AND METHODOLOGY

### 2.1. Materials

Beakers conical flasks, crucible, filter papers, pipettes, weighing balance, soxhlet extractors, measuring cylinder, centrifuge, electric grinder, syringes and needles, water-bath, sterile sample bottles, desiccators, steel cages, thermometer, 30 albino rats.

#### 2.1.1. Reagents/Chemicals

Alloxan monohydrate (St Louis M.O. USA), Cholesterol reagent (Teco Diagnostics USA), Triglyceride GPO reagent (Teco Diagnostics USA), HDL cholesterol reagent (Agape Diagnostic Switzerland), Insulin (Novolog, USA) and Atorvastatin (Unipex, USA).

#### 2.1.2. Plant Sample Collection

Fresh fruits of *Persea americana* were plucked from *Avocado* pear tree within the campus of Abia State Polytechnic, Nigeria. The plucked fruits were identified and authenticated by Dr. Ndukwe, Okorie (Botanist) of the Department of Biology in Abia State Polytechnic, Nigeria.

#### 2.1.3. Experimental Animals

Thirty (30) healthy adult of Albino Wistar rats (Weight range of 80-100mg) were obtained/purchased from the animal house of the University of Nigeria, Nsukka, Enugu State, Nigeria. The animals were kept in the animal house of the Department of Biochemistry, Abia State Polytechnic and were acclimatized for seven (7) days before the start of the experiment. The animals were housed separately in steel cages and were fed with water and grower mash at free access.

## 2.2. Methodology

### 2.2.1. Plant Sample Preparation

The succulent parts of the fruits (*Persea americana*) were removed to obtain the seeds. The seeds were dried and pulverized by grinding.

### 2.2.2. Preparation of Plant Extract

The powdered sample (50g) was macerated in 400ml of hot distilled water (40°C – 60°C) for 6hours and then filtered. The process was repeated each day throughout the period of the experiment.

### 2.2.3. Phytochemical Analysis of the Sample

Phytochemical analysis of dried powdered seed of *Persea americana* was carried out to identify the Phyto-constituents in the extract. The analytical procedures for alkaloids, saponins, tannins, flavonoids, steroids, phenols and cyanogenic glucosides, adopted were described by Ukpabi, et al. [13].

### 2.2.4. Induction of Diabetes

A single dose of a freshly prepared alloxan monohydrate in normal saline at a dose of 150mg/kg body weight was injected intraperitoneally into the rats. Blood samples were collected by tail vein tapping and was monitored for glucose levels using a glucometer. After 3 days, rats that had blood glucose levels above 250mg/kg were considered diabetic and were selected for study.

### 2.2.5. Experimental Design/Treatment

The animals were grouped into six groups of five animals per group as shown below:

Group A- (Normal control): This group was not intoxicated and was given access to food and water.

Group B- (Negative control): This group was induced with 1ml each of 150mg/kg alloxan Ip without treatment.

Group C- (Positive control 1): This group was induced with 1ml each of 150mg/kg alloxan Ip and treated with insulin (400mg/kg).

Group D- (Positive control 2): This group was induced with 1ml each of 150mg/kg alloxan Ip and treated with atorvastatin (30mg/kg).

Group E- (Test group 1): This group was induced with 1ml each of 150mg/kg alloxan Ip and treated with 200mg/kg of *P. Americana*.

Group F-(Test group 2): This group was induced with 1ml of 150mg/kg alloxan Ip and treated with 400mg/kg of *P. americana*.

Subsequently treatment regime of hyperglycemia and hyperlipidemia started on the 4<sup>th</sup> and 8<sup>th</sup> of the experiment respectively.

### 2.2.6. Collection of Blood Sample

After the administration of the sample, the animals were fasted for 6 hours. Blood samples were collected by cardiac puncture from each animal after mild anaesthesia with chloroform. The serum was separated from the blood after clotting and centrifugation for biochemical assay.

### 2.2.7. Biochemical Analysis

#### 2.2.7.1. Lipid Profile Assay

Triacylglycerol and total cholesterol were determined after enzymatic hydrolysis and the coloured complex measured by spectrophotometry. HDL was determined by the dextran sulphate Mg<sup>2+</sup> method and LDL was calculated using Friedewald equation according to Imafidon and Amaechina [14].

#### 2.2.7.2. Glucose Estimation

The glucose estimation was carried out using the glucose method via glucometer.

## 3. RESULTS

**Table-1.** Qualitative phytochemical constituent of aqueous extract of *Persea americana* (Avocado pear seed).

| S/N | Phytochemicals        | Presence |
|-----|-----------------------|----------|
| 1.  | Saponins              | +++      |
| 2.  | Tannins               | +        |
| 3.  | Flavonoids            | ++       |
| 4.  | Cyanogenic glycosides | +        |
| 5.  | Alkaloids             | ++       |
| 6.  | Phenols               | +++      |
| 7.  | Steroids              | +        |

**Note:** + = slightly present.  
++ = Moderately present.  
+++ = Strongly present.

### 3.1 Phytochemical Composition of Aqueous Seed Extracts of *Persea Americana*

Result obtained Table 1 showed that the aqueous extract of the dry powder of *Persea americana* seeds gave reactions for alkaloids, flavonoids, tannins, saponins, cyanogenic glycosides, phenols and steroids. Saponins and

phenols reaction gave the deepest colouration followed by flavonoids and alkaloids, and then tannins, steroids and cyanogenic glycosides.

### 3.2. Effect of Aqueous Seed Extracts of *Persea Americana* on Blood Glucose Concentration of Alloxan-Induced Albino Rats

Results obtained from the diabetic study Table 2 on albino rats with 80-100mg/kg body weight showed that the aqueous seed extract of *Persea americana* decreased blood glucose in a dose dependent fashion. Decrease in the blood glucose concentration was significant when compared to the negative control that received only normal feed and water.

**Table-2.** Serum glucose level of alloxan induced diabetic rats after treatment with insulin and aqueous seed extracts of *Persea Americana*.

| Group   | Initial BGL (mg/kg) | Day 4 BGL (mg/kg) | Day 8 BGL (mg/kg) | Day 12 BGL (mg/kg) |
|---------|---------------------|-------------------|-------------------|--------------------|
| Group A | 83.00 ± 2.30        | 83.40 ± 3.20      | 84.00 ± 1.98      | 85.50 ± 2.91       |
| Group B | 283.33 ± 1.34       | 268.58 ± 1.64     | 271.23 ± 1.15     | 266.85 ± 3         |
| Group C | 280.00 ± 1.34       | 210.25 ± 2.96     | 160.12 ± 1.33     | 100.13 ± 1.91      |
| Group E | 290.00 ± 4.44       | 220.55 ± 2.70     | 160.00 ± 1.60     | 108.00 ± 1.55      |
| Group F | 280.00 ± 2.60       | 209.60 ± 2.88     | 180.00 ± 2.06     | 90.00 ± 4.60       |

Note: Results are expressed as mean ± SEM (n=5).  
BGL=Blood Glucose Level.

### 3.3. Effect of Alloxan-Monohydrate Induction on Lipid Profile of Albino Rats

Intoxication of albino rats with alloxan-monohydrate produced evaluated lipid profile values in TG, TC, and LDL, which were significantly higher than the normal control, except HDL which was significantly decreased Table 3.

**Table-3.** Serum Lipid levels in rats following the induction of alloxan-monohydrate (150mg/kg).

| Group   | TG(mg/kg)    | TC (mg/kg)   | LDL (mg/kg) | HDL (mg/kg) |
|---------|--------------|--------------|-------------|-------------|
| Group A | 81.87±1.91   | 80.51±1.34   | 28.82±1.33  | 36.64±2.96  |
| Group B | 159.21± 1.51 | 149.89± 3.33 | 53.19± 2.67 | 25.53±1.59  |

Note: Results are expressed as mean ± SEM (n=5).

TG = Triglyceride.

TC = Total cholesterol.

LDL = Low density lipoprotein.

HDL = High density lipoprotein.

### 3.4. Effect of the Aqueous Seed Extracts of *Persea Americana* of Serum Lipid Profile on Diabetic Rats

Results obtained in Table 4 showed that serum TG, TC, and LDL concentrations in alloxan intoxicated animals were decreased towards the normal. Treatment with the extract also increased the HDL concentration towards the normal. The responses were in dose dependent-manner. The reference drug Atorvastatin was effective in TG and TC reduction while High dose aqueous seed extracts of *Persea americana* was effective in the treatment of LDL and HDL.

**Table-4.** Serum Lipid levels in rats following oral treatment of Atorvastatin (30mg/kg) and Aqueous seed extracts of *Persea Americana*.

| Group   | TG(Mg/dl)   |             | TC (mg/dl)  |             | LDL (Mg/dl) |            | HDL (mg/dl) |            |
|---------|-------------|-------------|-------------|-------------|-------------|------------|-------------|------------|
|         | 13 Days     | 18 Days     | 13 Days     | 18 Days     | 13 Days     | 18 Days    | 13 Days     | 18 Days    |
| Group D | 121.77±3.38 | 84.63±2.84  | 119.88±3.12 | 86.29±2.57  | 46.60±0.95  | 29.40±2.03 | 28.99±2.03  | 37.48±4.56 |
| Group E | 150.32±1.67 | 140.01±1.34 | 140.02±0.39 | 125.82±0.51 | 47.87±2.63  | 42.40±1.18 | 28.02±1.54  | 33.29±1.37 |
| Group F | 119.05±2.47 | 89.24±2.86  | 112.71±0.04 | 88.65±3.32  | 35.99±0.93  | 27.09±1.16 | 35.10±0.63  | 42.24±4.32 |

Note: TG = Triglyceride.

TC = Total cholesterol.

LDL = Low density lipoprotein.

HDL = High density lipoprotein.

#### 4. DISCUSSION

Plants produce a great variety of organic compounds that are not directly involved in primary metabolic processes of growth and development. These secondary organic compounds are referred to as phytochemical compounds. Medicinal actions of plants are unique to particular plant species or groups unlike the primary compounds such as carbohydrates, protein and lipids which are common to all plants [15]. The plant, *Persea americana* was found to contain certain phytochemical compounds such as flavonoids, tannins, saponins, alkaloids, phenols, steroids and cyanogenic glycosides Table 1 [16, 17]. Phenol and saponin contents of the extracts of *Persea americana* were shown to be appreciable. A number of plant biotechnology studies have demonstrated the presence of plant hormones including insulin-like hormones in germination, shoot and root development.

Insulin is a peptide hormone produced by beta cells of the pancreatic islets in human and it is considered to be the main anabolic hormone of the body. Its hypoglycemic effect is by signaling the liver, muscle and fat cells to take in glucose from the blood [3]. Insulin therapy is a critical part of treatment for people with type 1 diabetes and also for many with type 2 diabetes. The goal of insulin therapy is to maintain blood sugar levels within target ranges.

Alloxan monohydrate has been known to have selective pancreatic cell toxicity. It has been known to have widely used in the induction of diabetic mellitus in animals. Alloxan monohydrate is a beta cytotoxic which exerts its cytotoxic property through the destruction of beta-cells of islets located in the Langerhans of pancreas. This causes a decreased endogenous insulin secretion producing a decreased body tissue utilization of glucose. This causes an increase in blood glucose level coupled with elevation of serum levels of triglyceride and cholesterol [2]. The observed significant reduction in the serum concentrations of triglyceride, total cholesterol, LDL, with increase in HDL following oral administration of the aqueous seed extract of *Persea americana* could also be due to adequate control of the blood glucose concentrations Table 3. This observation may suggest that blood glucose homeostasis and the rate of lipolysis in adipose tissue are associated. Comparing the results of the insulin with those obtained from the plant extracts in this study, the 400mg/kg of the seed extract evoked the most hypoglycemic effect. Another observation arising from this study is the effect of atorvastatin compared with the seed extracts in the treated rats. Atorvastatin treated rats had lower reduction in TG & TC concentrations, while the seed extract (400mg/kg) had the same effect in LDL and HDL normalization, though not significant. This may be attributed to the fact that atorvastatin is primarily a competitive inhibitor of hydroxyglutanyl-coenzyme in cholesterol biosynthesis via the mevalonate pathway. Since literature has reported that there is a strong link between Diabetes mellitus and hyperlipidemia, this extract can therefore be used not only to control glucose homeostasis in diabetes but to control dyslipidemia alike [18].

#### 5. CONCLUSION

The findings of the study revealed that consumption of the aqueous seed extract of *Persea americana* exerts significant hypoglycemic effects on alloxan induced diabetic rats, with the hyperlipidemic benefits. Diabetes mellitus is one of the major chronic diseases caused by metabolism of carbohydrate, lipid, and protein. Despite numerous advanced researches in medicine, there is no satisfactory drug in treating diabetes mellitus. This study showed that *Persea americana* seeds have the valuable potentials for complementary therapy for the treatment of diabetes mellitus and its complications. The findings may support acclaimed traditional use of avocado pear seeds for controlling hyperglycemia in diabetes and its complications.

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