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Antidiabetic Effect of Methanol Extracts of *Telfairia Occidentalis* and *Persea Americana* Leaves on Streptozotocin induced Wistar Rats

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Abstract

This study was carried out to determine the antidiabetic effect of methanol leaf extract of Telfairia occidentalis and Persea americana leaves on Streptozotocin induced diabetic rats. The qualitative phytochemical screening of T. occidentalis and P. americana leaves were carried out using standard methods. Diabetes was induced in the animals by intraperitoneal injection of streptozotocin (50 mg/kg body weight) in 0.1 mol/L citrate buffer (pH 4.5). After 48 hours of the injection, rats that were diabetic (indicated by hyperglycemia) were used for the experiment. Blood samples were collected from the tails of the rats and blood glucose was determined using a glucometer. Thirty rats were divided into six groups of five rats each and treated with different doses of the extracts and compared with 0.25 mg/kg body weight of glibenclamide standard drug. The result showed that; Tannin, phenols and Saponins were found to be present in both T. occidentalis and P. Americana extracts. There was significant increase ($p<0.05$) observed in final weight of all treated groups and the control when compared to their initial weights. The doses of T. occidentalis and P. Americana methanol leaf extract (50 mg/kg body weight each) decreased significantly ($P<0.05$) the blood glucose levels in the diabetic treated group III and IV respectively when compared to the diabetic control group II. Significant decrease ($p<0.05$) were observed in serum levels of AST and ALT when compared to diabetic control. However, serum levels of ALP were significantly increased ($p<0.05$) in group III when compared to normal control and significantly decreased in groups IV and V treated rats. It can be concluded that T. occidentalis and P. americana are potential antidiabetic agents, the extracts were able to improve the serum AST, ALT and ALP of diabetic rats. The extracts were also able to prevent the weight lost and high blood glucose observed in diabetic untreated rats. Further research is therefore needed on these plants with the view to explore some possible active antidiabetic ingredients and their mechanism of action.

Keywords: Diabetes, Streptozotocin, *Glibenclamide,* ***Persea Americana, Telfairia Occidentalis*****, Serum.**

Introduction

Diabetes mellitus, a metabolic disease associated with relatively low or absolute deficiency of insulin secretion is the primary cause of diabetic kidney disease (DKD). Diabetic kidney disease progression as one of the critical problems resulting from diabetes mellitus is associated with complications

such as retinopathy, neuropathy, hepatopathy, nephropathy and cardiomyopathy, which are primary cause of morbidity and mortality worldwide (Adeshara *et al*., 2016; Arévalo-Lorido *et al*., 2016; Jagdale *et al*., 2016; Badal and Danesh, 2015).

Hyperglycemia-induced oxidative stress has been reported as one of the links between diabetes and diabetic complications ranging from endothelial dysfunction, insulin resistance, and alterations in the proportion and functions of pancreatic β -cells and ultimately leads to diabetic microvascular and macrovascular complications (Luo *et al*., 2016, Muhl *et al*., 2016). Hence, glucose oxidation, protein glycosylation and lipid peroxidation are as a result of free radical generation leading to increase the reactive oxygen species (ROS). Under physiological conditions, ROS plays an important role in cell signaling implicated in proliferation, differentiation, apoptosis, and immune defense in various cell types, as well as renal cells (Ozbek, 2012). However, oxidative stress associated with free radical generation and reactive oxygen species can be attributed to reduction in antioxidant activity. Both endogenous and exogenous antioxidants interact with these oxidants to counteract the oxidative damage to cells (Decoursey and Ligeti, 2005).

The role of the liver in metabolism, including detoxification, makes it particularly vulnerable to exogenous substances. In diabetes, liver damage may occur in the later stages of the disease due to disorders in lipid metabolism and increased gluconeogenesis and ketogenesis (Virdi *et al*., 2003). In addition, the oxidative stress imposed by both human and experimental diabetes may also result to multi-organ damage including liver damage (Kazeem *et al*., 2013).

Traditional medicines derived mainly from plants play an important role in the management of diabetes. Historically, plants have been used as sources of drugs administered empirically or otherwise in the cure of diseases. Plants were also allegedly used to treat diabetes. Although various plants have been employed in traditional medicine in Nigeria to treat diabetes, a lot still remains to be done scientifically to confirm the efficacy of these herbal drugs. Examples of plants in Nigeria with anti-diabetic properties includes; *Dioscorea dumetorum*, *Anthocleista vogelii*, *Loranthus begwensis*, *Catharantus roseus* (Ohadoma and Michael, 2011), *Ceiba pentandra* (Ladeji *et al*., 2003), *Solenostemon monostachys*, *Carica papaya*, *Musa paradisiaca* (Ojewole and Adewunni, 2003), *Ipomea batatas*, *Musa sapientum*, *Myrianthus arboreus*, *Emilia sonchifora* (Monago and Ugbomeh, 2004), *Allium cepa*, *Allium sativum* and *Zingiber officinale* (Ozougwu, 2017)

Telfairia occidentalis is a tropical vine grown in West Africa as a leaf vegetable and for its edible seeds. *Telfairia occidentalis* (*Cucurbitaceae*), is cultivated mainly in West Africa, especially in Nigeria, Ghana, and Sierra Leone (Onyeka *et al*., 2018). Fluted pumpkin (*Telfairia occidentalis*) is a creeping vegetative shrub that spreads low across the ground with large lobed leaves and long twisting tendrils (Onyeka *et al*., 2018). The leaves are cooked and eaten while the seeds which contain about 30% protein can be boiled and eaten, or ground into powder for soup. The seed can also be fermented for several days and eaten as slurry (Eseyin *et al*., 2005). The medicinal importance of the plant is being gradually investigated. *Telfairia occidentalis* is now known to possess anti-inflammatory effect (Oluwole *et al*., 2003), anti-bacterial activity

(Nwozo *et al*., 2004), erythropoietic value (Ajayi *et al*., 2000), anticholesterolemic and immune building properties (Eseyin *et al*., 2005).

Persea americana mill (*lauraceae*) is a tree named avocado or alligator pear. It is chiefly grown in temperate regions and sparsely grown in tropical regions of the world. *Persea americana* (pear) is reported to be high in ash crude fats, carbohydrate, energy, zinc, iron, manganese and magnesium (Kawagishi *et al*., 2001). They are also rich in bioactive substances such as phenols, alkaloids, Saponins and flavonoids and have been reported to possess anti-cancer, anti- microbial and hypoglycemic properties (Pradeep *et al*., 2012; Ezejiofor *et al*., 2013). *Persea americana* tree originated in South Central Mexico (Chen *et al*., 2008) and widely distributed throughout the tropical regions of the world. It is classified as a member of the flowering plant family *Lauraceae*. *P. americana* leaves have been reported to have anti-inflammatory and analgesic activities (Adeyemi *et al*., 2002). Also, the antidiabetic effect of the aqueous extract was reported (Antia *et al*., 2005).

Materials and Method

Equipment

Soxhlet apparatus (AVI8741; Mantle Type Soxhlet Extraction Heater, AVI Scientific (India))

Finely ground samples of *T. occedentalis* and *P. americana* were placed in a porous bag (thimble) made from a strong cellulose, which is placed in the thimble chamber of the Soxhlet apparatus. Extraction solvents was heated in the bottom flask, vaporizes into the sample thimble, condenses in the condenser and drip back. When the liquid content reaches the siphon arm, the liquid contents were emptied into the bottom flask again and the process is continued.

Top-loading balance (Apollo GX-A/GF-A Series; A&D Weighing, United States).

The weight of the dried samples (*T. occedentalis* and *P. americana*) and animals used in this study were taken using the top-loading balance. Dried samples were measured (50g) each. Rats were placed in a container after taking the weight of the empty container and their weights taken. The weight of powdered reagents was also taken using the top-balance.

Glucometer (One-Touch Horizon glucometer; Ortho-Clinical Diagnostics, Johnson and Johnson Company, USA). Glucose levels of rats were measured by applying a drop of serum blood to a chemically treated, disposable test-strip which was then inserted into a blood glucometer. The reaction between the test strip and the blood was detected by the meter and displayed in units of mg/dl.

To obtain serum for biochemical analysis, blood was collected aseptically after sacrifice via jugular vein. The blood was decanted into plain test tubes and allowed to stand for 30 minutes before centrifuged at 3000 × g for 10 min. Thereafter, serum was decanted into a micro tube and stored at -20 ^{0}C until analysed.

Analyzer (Robonik India Private Limited).

Blood samples stored in micro tubes at -20^{o}C were withdrawn and allowed to defreeze in a warmed water bath. Blood samples in micro tubes were placed in the auto analyzer for 30 minutes and the readings of ALT, AST and ALP were obtained for each sample.

Chemicals and Reagents

Streptozotocin (Sigma-Aldrich), Alpha-naphthol, Benedict reagent, Hager reagent (picric acid), Ninhydrin reagent. All other reagents are of analytical grade and purchased from reputable chemical company (AVI Scientific (India).

Collection of Samples

The leaves of *Telfairia occidentalis* and *Persea americana* were collected from Wuro-Gude market, Mubi North Local Government Area of Adamawa State, Nigeria.

Experimental Animals

Forty male Sprague-Dawley rats, weighing 120–180 g, was obtained from National Research Institute, Vom, Jos, Plateau State. Guidelines for the care and use of laboratory animals was approved by the local ethics committee at the Adamawa State University Mubi. Rats were housed in wire-floored cages under a 12 h light–dark cycle for 7 days prior to treatment and were fed with standard laboratory chew and tap water ad libitum.

Induction of Diabetes

This was done as described by Rajendran *et al*., (2014) with little modification. Animals were fasted overnight and diabetes was induced by a single intraperitoneal injection of a freshly prepared solution of STZ (50 mg/kg bd.wt.) in 0.1 mol/L citrate buffer (pH 4.5). The dosing volume was 1 ml/kg. To prevent fatal hypoglycemia, rats were kept on 5% glucose solution for 24 h after STZ injection. Successful induction of diabetes was confirmed by measuring the fasting blood glucose concentration in rats 6 h after injection of STZ. Rats with a fasting blood glucose level > 200 mg/dl were considered diabetic and included in the study (Rajendran *et al*., 2014).

Experimental Design

This was done as described by Mooradian *et al*., (2005). Forty-eight hours after the administration of STZ and citrate buffer, control and diabetic rats were randomly assigned to treatments with *Telfairia occidentalis* and *Perssea americana* leaves extracts. Thirty rats were divided into six groups, with five rats in each group, and treated as follows for three (3) weeks:

Group I: normal control rats receiving (citrate buffer; 1 ml/kg/day)

Group II: diabetic control rats receiving (citrate buffer; 1 mg/kg/day) aqueous solution daily via an intragastric

Group III: diabetic rats + 50 mg/kg bd.wt. of *P. americana* treatment

Group IV: diabetic rats + 50 mg/kg bd. wt. of *T. occidentalis* treatment

Group V: diabetic rats + 50 mg/kg bd.wt. of *P. americana* + 50 mg/kg b.w. of *T. occidentalis*.

Group VI: diabetic rats + 0.25mg/kg Glibenclamide standard drug (Mooradian *et al*., 2005).

The following parameters were assessed in each of the study groups during the treatment period: final body weight and blood glucose concentration were determined by measuring weight on weighing balance and blood glucose using glucometer. After the last treatment (3 weeks), rats were fasted overnight and sacrificed by cervical decapitation. Blood was collected in tubes, without anticoagulant, for the estimation of serum activities of Alanine Transaminase (ALT), Aspartate Transaminase (AST) and alkaline phosphatase (ALP).

Biochemical Assessment

Serum activities of Alanine Transaminase (ALT), Aspartate Transaminase (AST) and alkaline phosphatase (ALP) were determined by a standard automated technique using Hitachi Analyzer. These

was investigated at General Hospital Mubi, Adamawa State at the Biochemistry analysis unit.

Statistical Analysis

All data were expressed as mean ± S.D. Data were analyzed by One-way analysis of variance using Statistical Package for Social Sciences (SPSS) version 26.0. Difference between groups was compared by Dunett's Post hoc test and $P < 0.05$ was selected as the level of statistical significance.

Results and Discussion

In this study, the qualitative phytochemical screening of *Telfairia occidentalis* and *Persea americana* showed that their leaves contain tannins, phenols and Saponins while alkaloids, and steroids were absent (Table 1). Secondary metabolites (flavonoids, N-containing compounds, and terpenoids) of plants possess some alpha-glycosidase inhibitors and competitively inhibit intestinal brush border enzymes with an eventual reduction in digestion and absorption of carbohydrates from the gut-postprandial hyperglycaemia, hence resulting in an effective glucose control (Nimenbo-Uadia, 2003).

Significant decreases ($p<0.05$) were observed at the end of the period of administration in final weights of treated groups 3, 4, 5 and 6 when compared with the initial weights, while there was significant increase ($p<0.05$) observed in final weight of diabetic control compared with the initial weight (Table 2). The loss in weight observed in the treated groups could be the extracts might have caused loss of appetite in the animals and obviously due to the inability of peripheral tissues to uptake metabolites from the bloodstream. Factors responsible for weight lost in diabetes include proteolysis, lipolysis and acute fluid loss (Tiwari and Rao, 2002).

The most common biochemical marker used in the diagnosis and progress monitoring during management of diabetes mellitus in clinical and experimental settings is blood and/or serum glucose concentration (Luka *et al*., 2013). Results in Table 3 shows the mean blood glucose concentrations of the control groups (normal and diabetic controls), the dose of the *P. americana* and *T. occidentallis* methanol leaf extract and the standard drug (glibenclamide). The doses of *P. Americana* and *T. occidentalis* methanol leaf extract decreased significantly ($P<0.05$) the blood glucose levels in the diabetic treatment group 3 (208.66 ± 0.17) and 4 (207.00 ± 0.05) respectively when compared to the diabetic control group (232.00 ± 0.50). Also, in the streptozotocin-induced diabetic group treated with glibenclamide (202.00 ± 0.14), a significant decrease ($p<0.05$) was observed in the blood glucose concentrations when compared to the diabetic control group (232.00 ± 0.50). Blood glucose concentrations were measured in this study and results showed significant reduction ($p<0.05$) in blood glucose of diabetic rats treated with methanol extracts of *P. americana and T. occidentallis*. Extracts also competed with the reference drug glibenclamide. However, combined effect of the two extracts (*P. americana and T. occidentallis*) was better in expressing this hypoglycemic potential.

Significant decrease ($p<0.05$) was observed in serum levels of AST and ALT when compared to diabetic control (Table 4). However, serum levels of ALP were significantly increased ($p<0.05$) in group 3 (treated with *P. americana* extract) when compared to normal control and significantly decreased in group 4 and 5 treated rats. ALT and AST are cytosolic enzymes that can be used to assess damage to the liver and heart (Yakubu *et al*.,

2008). The increase in the serum enzymes is quite understandable since disruption of the plasma membrane of the organs of the animals will be accompanied by leakage of these cytosolic enzymes into the serum, hence, the observed increase in the level of the enzymes in the serum (Akanji and Yakubu, 2000). Alkaline phosphatase (ALP) is a marker enzyme of damage for the plasma membrane and endoplasmic reticulum (Shahjahan *et al*., 2004). It is frequently used to assess the integrity of the plasma membrane (Yakubu *et al*., 2008). Enzymes from diseased or damaged tissues may become recognizable in the serum presumably by leakage through altered cell membrane of the rat organs (Yakubu *et al*., 2007). The increase in serum ALP activities following the oral administration of the methanol extracts implies damage to the plasma membrane (Yakubu *et al*., 2003). Such increase in the activities of the enzymes suggests disruption of the ordered lipid-bilayer of the membrane structure of the affected organs.

Table 1: Qualitative Phytochemical Analysis for *Telfairia occedentalis* and *Persea americana* Methanol leaves Extracts

Phytochemicals	*Telfairia occidentalis*	*Persea americana*
Alkaloids	-	+
Tannins	+	-
Phenols	+	-
Saponins	-	+
Steroids	-	+

Keys: (+) = present, (-) = absent

Table 2: Effects of Methanol Leaves Extract of *Telfairia occedentalis* and *Persea americana* on Body Weight (g) of rats

Groups	Treatment	Initial	Final
I	Normal Control	121.33 ± 0.05^{a}	135.33 ± 0.14^{b}
II	Diabetic control	129.66 ± 0.10^{a}	147.00 ± 0.10^{c}
III	DI + *P. americana* (50 mg/kg)	128.66 ± 0.30^{b}	115.00 ± 0.25^{a}
IV	DI + *T. occidentallis* (50 mg/kg)	132.50 ± 0.05^{b}	116.50 ± 0.10^{a}
V	DI + *P. am*. (50mg/kg) + *T. oc*. (50mg/kg)	131.50 ± 0.25^{c}	106.50 ± 0.20^{b}
VI	DI + Glibenclamide (0.25 mg/kg)	133.50 ± 0.10c	116.50 ± 0.25^{b}

Values are mean ± SD. Values with the same superscript are statistically not significant ($p<0.05$).

Table 3: Effects of Methanol Leaves Extract of *Telfairia occedentalis* and *Persea americana* on Blood Glucose Level (mg/dl) of rats

Groups	Treatment	Initial	Final
I	Normal Control	114.66 ± 0.51^{a}	123.66 ± 0.10^{b}
II	Diabetic control	226.66 ± 0.30^{b}	232.00 ± 0.50^{b}
III	DI + *P. americana* (50 mg/kg)	223.66 ± 0.05^{b}	208.66 ± 0.17^{a}
IV	DI + *T. occidentalis* (50mg/kg)	223.00 ± 0.10^{b}	207.00 ± 0.05^{a}
V	DI + *P. am*. (50mg/kg) + *T.oc*.(50mg/kg)	221.50 ± 0.14^{a}	191.00 ± 0.20^{a}
VI	DI + Glibenclamide (0.25 mg/kg)	224.50 ± 0.11^{b}	202.00 ± 0.14^{a}

Values are mean ± SD. Values with the same superscript across the row are statistically not significant ($p<0.05$).

Table 4: Effects of Methanol Leaves Extract of *Telfairia occedentalis* and *Persea americana* on Serum Biochemical Parameters (U/L) of rats

Groups	Treatment	AST (U/L)	ALT (U/L)	ALP (U/L)
I	Normal Control	3.01 ± 0.05^{a}	6.82 ± 0.05^{b}	3.21 ± 0.10^{a}
II	Diabetic control	12.85 ± 0.01^{b}	11.61 ± 0.10^{a}	11.90 ± 0.01^{b}
III	DI + *P. americana* (50mg/kg)	8.07 ± 0.13^{c}	6.31 ± 0.18^{b}	8.02 ± 0.05^{b}
IV	DI + *T. occidentallis* (50mg/kg)	7.62 ± 0.42^{c}	5.80 ± 0.07^{b}	5.60 ± 0.10^{a}
V	DI + *P. am.*(50mg/kg) + *T.oc.*(50mg/kg)	6.78 ± 0.50^{c}	5.42 ± 0.14^{b}	4.91 ± 0.05^{a}
VI	DI + Glibenclamide (0.25 mg/kg)	9.02 ± 0.34^{bc}	8.87 ± 0.50^{ab}	7.67 ± 0.31^{ab}

Values are mean ± SD. Values with the same superscript across the column are statistically not significant ($p<0.05$).

Conclusion

Results from this study reveals the hypoglycemic properties of methanol extracts of *Persea americana* and *Telfairia occidentallis*. The hypoglycemic effect of the extracts competed with the reference drug glibenclamide. The extracts were able to improve the serum AST, ALT and ALP of diabetic rats.

Consent

It is not applicable.

Competing Interests

Authors have declared that no competing interests exist.

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