World Journal of
Biological and Pharmaceutical Research

Journal homepage: https://zealjournals.com/wjbpr/

ISSN: 2799-0338 (Online)

(RESEARCH ARTICLE)

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Effect of acute and chronic administration of hot water extract of *P. Americana* on some metabolic parameters in diabetic rats

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World Journal of Biological and Pharmaceutical Research, 2022, 03(02), 001–009

Publication history: Received on 01 October 2022; revised on 05 November 2022; accepted on 08 November 2022

Article DOI: https://doi.org/10.53346/wjbpr.2022.3.2.0041

Abstract

The challenge of comorbid diseases and especially their management. Posing greater challenge are phytomedical approach without proper scientific testing and more also paucity of modern equipment for research and funding. The need to authenticate medicinal herbs used in the management of Diabetes Mellitus (DM) as one of the common metabolic diseases becomes imperative. This study aimed at evaluating the effect of acute and chronic administration of hot water extract of *P. americana* on some metabolic parameters in diabetic rats.

Thirty young adult healthy male albino rats (wistar strain) weighing between 205-251 g were made diabetic by administration of 80 mg/kg streptozotocin (STZ). The animals were divided into two equal groups of 15 rats each, singly placed in metabolic cages for the acute and chronic treatments studies. The rats were further divided into three groups of 5 animals each and treated with different concentrations of stem-bark hot water extract of Persea americana (HWE-PA) and distilled water while the body weight, food intake, faecal output, water intake and urine output were measured and recorded daily for a period of 5 days for the acute and 28 days for the chronic treatments. Results showed a higher percentage change in body weights, higher food intake and faecal output and lower values in water intake and urine output in both acute and chronic administration of HWE-PA to STZ-induced hyperglycaemic rats compared to the control groups. Both acute and chronic administration of Hot water extract of the stem-bark animals extracts of *Persea americana* (HWE-PA) presented antidiabetic activity STZ-induced hyperglycaemic rats as evident its ameliorating effect on the body weight, food intake, faecal output, water intake and urine output in STZ-induced hyperglycaemic rats, thus supports its phytomedicine use as an antidiabetic agent.

Keywords: Body weight; Food intake; Water intake; Faecal output; Urine output

1. Introduction

Metabolic syndrome represents a cluster of metabolic abnormalities that include hypertension, central obesity, insulin resistance and atherogenic dyslipidemia, and is strongly associated with an increased risk for developing diabetes and atherosclerotic and nonatherosclerotic cardiovascular disease [1]. It is estimated that there are approximately 250,000 higher plant species worldwide, out which only a few have been screened for pharmacological activity according to their traditional use [2]. The use of plants to cure several kinds of human diseases has a long history. Various parts of plants

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such as leaf, stem, bark, root, etc. are being used to prevent, allay symptoms or revert abnormalities back to normal [3]. Metabolic syndrome (MS) is a combination of clinical and biological abnormalities which confers greater risk of type 2 diabetes (T2DM), cardiovascular disease (CVD) [4] and liver diseases [5]. Report from prospective study involving 10,806,716 adults showed that changes in MetS and its components were associated with the risk of incident T2D [6]. Akande (2016), reported that Diabetes is an international public health issue. International Expert Committee recommended an alternative diagnostic index testing for diabetes using glycated (A1c) [7]. Defects in secretion of insulin manifesting as DM is one of the markers of the metabolic disorder. T2DM (adult-onset diabetes mellitus) caused by the resistance of insulin with increased pancreatic insulin therefore, insulin fails to maintain body metabolism [8]. Experimentally, streptozotocin (STZ) is often used to induce DM in animal models as causes the destruction of β-cells of islets of Langerhans resulting in the elevation of blood glucose levels [9, 10]. In animal models, the injection of STZ (45 mg kg^{-1}) to induce type 1 DM is a well-established model known to reduce the production of insulin without the need for exogenous administration of this hormone for animal survival [11, 12].

Wide spread use of herbs throughout the globe has raised serious concerns over its quality, safety, and efficacy. Thus, exact scientific assessment has become a precondition for acceptance of herbal health claims [13]. *Persea americana Mill.* (*Lauraceae*) is a subtropical tree with several medicinal potentials that have been exploited in folkloric medicine [14]. This tree is also known as "Avocado "can be tall or spreading, and they have elliptic to egg-shaped leaves that are 10–30 cm (4–12 inches) in length [15]. The tree is known only for the fruit that people usually consume. Apparently avocado leaf is one of the natural ingredients that can be used as a traditional medicine [16]. Various parts of Persea americana (*P. americana*) have been reported in many studies to be used by people from tropical countries to manage some health problems such as diarrhea, dysentery caused by helminths and amoebas, toothache, intestinal worms, diabetes, skin rashes, infectious processes caused by fungi and bacteria, asthma, high blood pressure and rheumatism, malaria and typhoid fever; to lower high blood cholesterol, to stimulate uterine contractions and to ease painful menstruations [17-21]. The leaves of Persea americana have been popularly used in the treatment of diabetes in countries of Latin America and Africa [22]. This study aimed at evaluating the effect of acute and chronic administration of hot water extract of *P. americana* on some metabolic parameters in diabetic rats.

2. Material and methods

2.1. Plant Material Collection, Preparation and Extraction

Fresh sample of Avocado plant was collected from Du District of Jos, South LGA, North-Central Nigeria. It was identified and classified at the Collee of Forestry, Jos, Nigeria. Subsequently, Stem-bark of the plant were collected, washed with clean water and dried at room temperature in the Pharmacology Laboratory of the Department of Pharmacology and Therapeutics, College of Medicine and Allied Health Sciences, Bingham University, Jos Campus, Nigeria. The dried plant material was further ground into powder.

Figure 1 *Persea americana* plant [23]

2.2. Hot Aqueous Crude Extraction of Plant Sample

A hundred grams (100 g) of the powdered stem bark of *P. americana* were respectively weighed loaded into different thimbles and fixed two different Soxhlet extractors with lagged glass wool sidearm. The Soxhlet extractor and condenser

was then fixed to a round bottom flask containing distilled water (1000 ml) placed on a six-channel heating mantle and adjusted for hot water extraction temperature of 60 ℃. On completion of the process, the extract was dried in a rotary evaporator, weighed and stored at -4 ℃ in a refrigerator until use. These were done according to the methods of [24 - 26].

2.3. Experimental animal procurement and protocols

Young adult healthy male albino rats (wistar strain) weighing between 205-251 g were sourced from the Animal House of the Department of Pharmacology of University of Jos, Nigeria. The rats were acclimatized for 7 days, maintained with pelleted feed, clean water and conducive environment according to required best practices as recommended by Tuhin RH *et al*., 2017 [27].

2.4. Induction of diabetes and acclimatization

The animals were fasted overnight but with access to clean drinking water *ad libitum* and then made diabetic by administration of 80 mg/kg streptozotocin (STZ) used in 0.1 M sodium citrate buffer, pH4.5 via intraperitoneal (*i.p.)* route as a single dose. Fasting Blood Glucose concentration (FBG) of each animal from venous blood sample was measured using One Touch Ultra glucometer (Accu-Check Active, Roche) after 24hours in order to confirm sustained hyperglycemic status. The rats with BGC (Blood glucose concentration) > 16.7 to 33.3 mmol/L (300–600 mg/dl) were considered diabetic according to the method described by Ogundeko *et al.,* 2022 [10] but with slight modification.

Thirty confirmed-hyperglycemic rats were divided into two equal groups of 15 rats each, singly placed in metabolic cages for the acute and chronic treatments studies and allowed 48 hours and 3 days respectively to stabilize in the cage environment.

2.5. Acute treatment studies

A total of 15 rats were randomly allocated in three groups of 5 animals each. The animals were put singly in metabolic cages and allowed 48 hours to acclimatize in the cage environment. They were then given single doses of the extracts as outlined below:

Group I – Equi-volume of distilled water and Group II – 750 mg/kg (i.p) HWE-PA (Hot water extract of *P. americana*).

The following parameters were measured and recorded daily for a period of 5 days:

- Body weight (g),
- Food intake (g),
- Water intake (ml),
- Facial output (g) and
- Urine output (ml).

The changes in these parameters (expressed in appropriate units) were plotted against time and effects observed compared with the animals in Group I (control).

2.6. Chronic treatment studies

Fifteen (15) rats were again randomly allocated in three groups and individually placed in metabolic cages allowing three days for acclimatization. From day zero, animals were treated daily as outlined below for a period of 28 days.

Group I - Equi-volume of distilled water and Group II – 250 mg/kg (i.p) HWE-PA daily.

The changes in the aforementioned metabolic parameters (also expressed in appropriate units) were plotted against time and the effects observed compared with the animals in the control (group I).

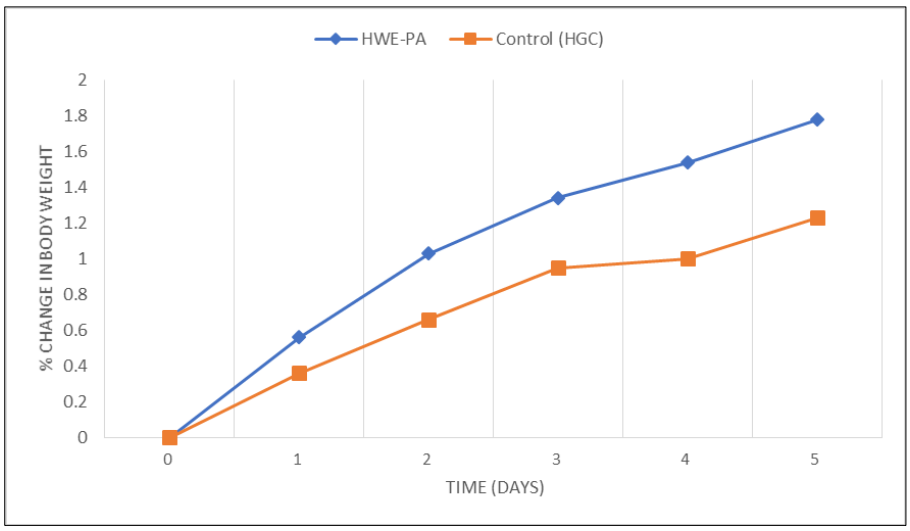
2.7. Statistical Analysis

Results from both acute and chronic treatments were expressed as mean ± SEM. Data was analyzed using the SPSS version 20 (SPSS Inc., Chicago, IL) statistical package and difference between mean of treated and control was considered significant if the value P was ($P \leq 0.05$) using One-way ANOVA test.

3. Results and discussion

3.1. Effect of acute and chronic administration of HWE-PA on some metabolic parameters of STZ-induced hyperglycemic rats

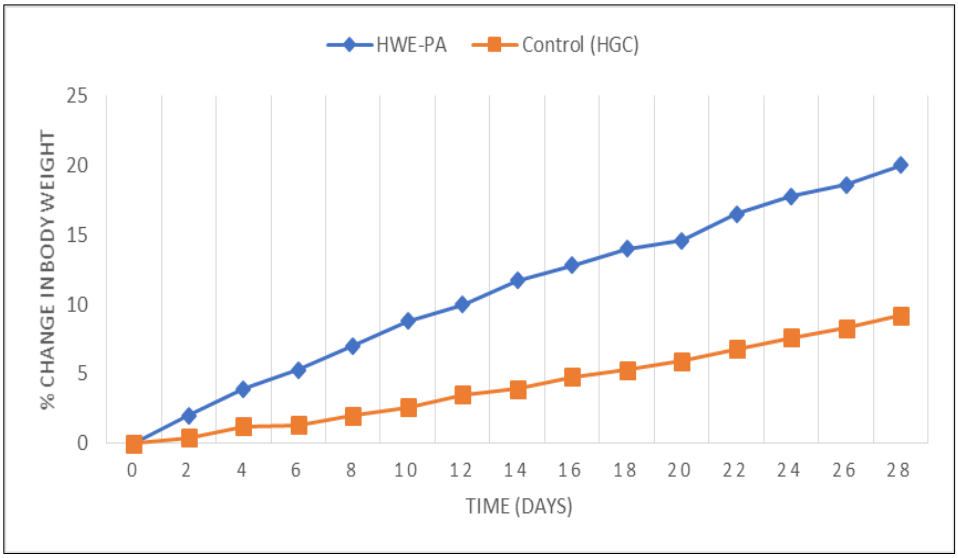
In the course of this study, various physical parameters, including body weight, food intake, faecal output, water intake and urine output were observed. Following acute treatment with a single large dose of HWE-PA (750 mg/kg i.p), the percentage change in body weights of HWE-PA treated animals was appreciably higher than for control animals – Figure 2.



*P<0.05 versus corresponding control, n = 5, +% Change = increase in body weight, -% Change = decrease in body weight, HGC = Hyperglycaemic control group; HWE-PA = Hot water extract of *P. Americana*

Figure 2 Effect of acute administration of HWE-PA on body weight of STZ-induced hyperglycaemic rats

3.2. Effect of chronic administration of HWE-PA on some metabolic parameters of STZ-induced hyperglycaemic rats



*P<0.05 versus corresponding control, n = 5, +% Change = increase in body weight, -% Change = decrease in body weight, HGC = Hyperglycaemic control group; HWE-PA = Hot water extract of *P. Americana*

Figure 3 Effect of chronic administration of HWE-PA on body weight of STZ-induced hyperglycaemic rats

Following daily treatment with HWE-PA, the percentage increase in body weights of the treated animals was consistently higher than that for the hyperglycaemic control animals – Figure 3.

This higher percentage change in body weights by way of increase in both acute and chronic administration of HWE-PA to STZ-induced hyperglycaemic rats compared to the control group (*Figures 2 and 3*) suggests an increase in glucose metabolism, the structural buildup of proteins as an alternate energy source or fat catabolism. In general, body weights of animals with diabetic status decreases. In order words, both acute and chronic administration HWE-PA may have may promoted insulin production from the residual β-cells or restored β-cells which could activate the hormones involved in fat storage in the STZ-induced hyperglycaemic rats. This is in consonance with the report by Ojo *et al*., 2022 [28].

Table 1 Effect of acute administration of HWE-PA on food intake and faecal output of STZ-induced hyperglycemic rats

Time (Days)	Control (HGC)		(HWE-PA)	
	Food Intake	Faecal Output	Food Intake	Faecal Output
1	3.1±0.06	2.4±0.09	3.8±0.72	2.1±0.17
2	3.7±0.02	3.0±0.06	5.0±0.57	3.9±0.21
3	4.6±0.05	3.3±0.03	6.3±0.82	5.8±0.69*
4	4.9±0.11	3.8±0.07	6.9±0.69	7.6±0.93*
5	5.3±0.1	4.0±0.16	7.2±0.56	8.9±0.68*

*P<0.05 versus corresponding control, n = 5, HGC = Hyperglycaemic control group, HWE-PA = Hot water extract of *P. Americana*

The HWE-PA treated and control animals however showed steady increase of food intake and faecal output – *Table 1*.

Table 2 Effect of chronic administration of HWE-PA on food intake and faecal output of STZ-induced hyperglycaemic rats

Time (Days)	Control (HGC)		(HWE-PA)	
	Food Intake	Faecal Output	Food Intake	Faecal Output
0	3.1±0.07	2.5±0.09	3.55±0.6	2.1±0.45
5	4.05±0.05	3.2±0.16	4.4±0.95	3.6±0.71
10	4.7±0.14	4.05±0.41	5.8±0.82	5.0±0.85
15	5.7±0.11	4.55±0.69	6.8±0.11	6.1±0.93
20	6.2±0.82	4.7±0.18	8.0±0.84*	7.3±0.91*
25	7.1±0.46	5.0±0.28	9.0±1.2*	7.6±0.98*
30	7.9±1.12	5.1±0.61	9.4±1.8*	8.2±1.4*

*P<0.05 versus corresponding control, n = 5, HGC = Hyperglycaemic control group, HWE-PA = Hot water extract of *P. Americana*

The food intake and faecal output of animals treated with HWE-PA was consistently higher than values for hyperglycaemic control animals throughout the study – *Table 2*.

A deficiency of insulin secretion leads to increased blood glucose levels and organ damage, which further disrupts the metabolism of the three major nutrients, namely, lipids, carbohydrates, and proteins [29, 30].

Our study further shows that the food intake and faecal output of animals treated with HWE-PA was consistently higher than values for hyperglycaemic control animals throughout the study.

The consistently higher food intake and faecal output as a result of the effect of acute and chronic administration of HWE-PA in the STZ-induced hyperglycaemic rats than those of the control animals suggests a compelling antidiabetic effects of the HWE-PA in the STZ-induced hyperglycaemic rats by way of reduced fasting, post-prandial hyperglycemia and improved metabolic parameters, including polydipsia and polyuria. This is tandem with a report on a plant extract by [31].

Table 3 Effect of acute administration of HWE-PA on water intake and urine output of STZ-induced hyperglycaemic rats

Time (Days)	Control (HGC)		(HWE-PA)	
	Water Intake	Urine Output	Water Intake	Urine Output
1	2.4±0.41	2.2±0.49	2.6±0.36	0.9±0.06
2	8.0±0.98	4.4±0.86	4.5±0.61*	2.3±0.38
3	11.2±1.02	6.8±0.97	6.4±0.58*	3.4±0.44*
4	14.4±1.66	8.3±1.08	8.2±1.01*	4.0±0.72*
5	17.9±2.06	10.1±1.14	8.4±1.26*	5.2±0.85*

*P<0.05 versus corresponding control, n = 5, HWE-PA = Hot water extract of *P. Americana*

Periodic 12 hourly water intake for animals treated with HWE-PA was lower than corresponding values for control animals – *Table 3*. Same trend was observed for the urine output. Thus, there was corresponding lower water intake and urine output for animals treated with HWE-PA – *Table 3.*

Table 4 Effect of chronic administration of HWE-PA on water intake and urine output of STZ-induced hyperglycaemic rats

Time (Days)	Control (HGC)		(HWE-PA)	
	Water Intake	Urine Output	Water Intake	Urine Output
0	8.2±0.64	0	7.2±0.35	0
5	11.8±0.92	2.0±0.11	8.9±0.73	1.0±0.24
10	14.1±1.02	3.6±0.34	11.0±1.04	2.0±0.19
15	16.6±1.86	5.3±0.65	11.8±1.68*	3.0±0.36
20	19.1±1.90	6.5±0.46	12.6±1.03*	3.5±0.49
25	20±1.03	7.5±0.92	13.8±1.67*	4.0±0.82
30	20.4±2.04	8.2±0.64	13.6±1.98*	4.2±0.38

*P<0.05 versus corresponding control, n = 5, HWE-PA = Hot water extract of *P. Americana*

Water intake for HWE-PA treated animals was lower than values for control animals throughout the study. Same trajectory was followed in the urine output values – *Table 4.*

The main function of the kidneys is to excrete the waste products of metabolism and to regulate the body concentration of water and salt. STZ administration elevated renal markers, i.e., serum urea nitrogen, creatinine, urine albumin, urine glucose, and urine protein and decreased urine urea and urine creatinine which are found responsible for proper maintenance, functioning of kidney, and change in the glomerular filtration rate [32, 33]. Hyperglycemia increases the generation of free radicals by glucose auto-oxidation and the increment of free radicals may lead to kidney cells damage [34]. From our study, same trend of lower values in water intake and urine output as a result of the effect of acute and chronic administration of HWE-PA on STZ-induced hyperglycaemic rats than those of the control animals throughout the study (*Tables 3 and 4*) suggests the antidiabetic activity of HWE-PA which may be through several mechanisms, including renal glucose reabsorption, insulin degradative processes inhibition, stimulation of beta cells of islets of Langerhans for insulin secretion, decrease the resistance of insulin, and regenerating or repairing the pancreatic beta cells by increasing the size and number of the cells in islets of Langerhans as reported by [35].

Herbs are a source of novel pharmaceuticals not only due to their potent efficacy with fewer side effects, but also due to the complex bioactive compounds they contain [36]. There is growing interest in the use of plant-derived bioactive compounds (e.g., herbal medicine) that could be potentially useful for different therapeutic purposes when treating this disease [37]. The phytochemical screening of the stem bark extracts of *P. americana* revealed the presence of bioactive compounds, including alkaloids, flavonoids, saponins, reducing sugars and tannins [38].

Saponins were known to be bioactive against diabetes [39]. Various reports have it that hypoglycemic action of saponin is via rejuvenation of insulin [40], amendment insulin signaling [41], release insulin from the beta cell islets [42], inhibition the activity of disaccharide [43], activation of glycogen synthesis [44], Inhibition of gluconeogenesis [45], inhibition the activity of α-glucosidase [40], inhibition of mRNA expression of glycogen phosphorylase and glucose 6-phosphatase [46] and increase the expression of Glut4

4. Conclusion

Both acute and chronic administration of Hot water extract of the stem-bark animals extracts of *Persea americana* (HWE-PA) presented antidiabetic activity STZ-induced hyperglycaemic rats as evident its ameliorating effect on the body weight, food intake, faecal output, water intake and urine output in STZ-induced hyperglycaemic rats, thus supports its phytomedicine use as an antidiabetic agent.

Compliance with ethical standards

Acknowledgments

The authors wish to appreciate the various support and assistance from Mrs. Lois Kamoh of Animal House Unit, Mr. F. Meshack, Mr. Tim and Grace Michael Anayi of the Department of Pharmacology and Therapeutics, Bingham University, Jos Campus.

Disclosure of conflict of interest

Authors declare no conflicting interest.

Statement of ethical approval

Mrs. L Kamoh and authors TOO and PNO are licensed to handle Laboratory animals and carry out Laboratory procedures involving Laboratory animals. Ethical principles governing the conduct of experiments with animal was maintained.

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