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Effect of acute and chronic administration of *Persia americana* (chloroform extract of stem bark) on blood glucose concentration of normoglycaemic and streptozotocin-induced hyperglycaemic mice

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Abstract

The effect of acute and chronic administration of the chloroform extract of the stem bark of P. americana on the blood glucose concentration (BGC) of normoglycaemic and streptozotocin (STZ)-induced hyperglycaemic mice was investigated. Firstly, fifteen (15) young albino mice allocated into three groups of five animals each after a 12 hour overnight fast were treated as follows: group 1 – equi-volume of distilled water, group 11- a single acute dose of 1200 mg/kg IP chloroform extract of P. americana (equivalent to 75% of LD_{50}) and group 111 – 20 mg/kg IP tolbutamide. Immediately after treatment, BGC was measured at 0, ½, 1, 2, 4, and 8 hrs. Secondly another population of 15 animals were shared into 3 groups of 5 animals each. Animals in group 1 were administered equi-volume of distilled water daily, group 11 and group 111 400 mg/kg IP (equivalent to 25% of LD_{50}) extract of *P. americana* and 10 mg/kg IP of tolbutamide respectively daily for twenty- five days. BGC was measured on days 1, 5, 10, 15,20, 25. Changes in BGC of normoglycaemic and STZ-induced hyperglycaemic mice as a result of acute and chronic administration of extract was compared with values for tolbutamide (positive control) and distilled water (negative control).

Results show that in normoglycaemic mice unlike the acute dose of 20 mg/kg IP reference drug tolbutamide, an acute dose of the extract (1200 mg/kg IP) did not significantly lower BGC. In the STZ-induced hyperglycaemic mice however, both the extract and the reference drug tolbutamide significantly lowered the BGC. With chronic administration both the extract and the reference drug significantly lower BGC in STZ-induced hyperglycaemic mice. It can be concluded therefore that acute and chronic administration of the chloroform extract of *P. americana* does have a hypoglycaemic activity only in STZ-induced hyperglycaemic mice. This may support the use of the stem bark of *P. americana* in the treatment of Diabetes mellitus.

Keywords: *Persia americana*; Normoglycaemia; Hyperglycaemia; Hypoglycaemic activity; Diabetes mellitus; Blood glucose concentration

1. Introduction

Persia americana is a tree which is native to the highland regions of south-central Mexico to Guatemala and well known for its medicinal use against dysentery, coughs, high blood pressure, liver problems, gout and aphrodisiac [1]. Over the past decades, herbal medicine has become a thing of global significance with medicinal and economic implications. Wide

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spread use of herbs throughout the globe has raised serious concern over its quality, safety and efficacy [2]. Thus, exact scientific assessment has become a precondition for acceptance of herbal health claims [3]. *P. americana* as a tree is also cultivated in tropical and subtropical climates around the world, belonging to the family *Lauraceae*, is widely used in Ayurveda and evidence-based phototherapy [4]. The World Health Organization (WHO) estimates that 4 billion people, 80% of the world population, presently use herbal medicine for some aspect of primary health care [5]. Many drugs commonly used today are of herbal origin because of their safety, quality and efficacy. Indeed, about 25% of the prescription drugs dispensed in the USA contain at least one active ingredient derived from plant material [6]. In Nigeria, most herbal concoctions used for the local treatment of diabetes contain extracts of *P. americana* amongst other herbs and hence the need to appraise the hypoglycemic property of the herb [7]. Persia americana is used in traditional medicine for the treatment of various ailments, such as menorrhagia, hypertension, hepatitis, stomach ache, diarrhea and bronchitis [8]. Diabetes mellitus is one of the major health problems in Nigeria, the incidence and associated mortality are increasing [9]. Inadequate regulation of blood sugar imposes serious consequences for health. Conventional antidiabetic drugs are effective; however, they are fraught with unavoidable side effects [10]. On the other hand, medicinal plants may act as an alternative source of antidiabetic agents especially where equi-effective [10]. *Persea americana*, commonly known as avocado, has recently gained substantial popularity and is often marketed as a "superfood" because of its unique nutritional composition, antioxidant content, and biochemical profile. Bhuyan DJ, 2019 [11]. Although the acute toxicity test (LD_{50}) has been widely criticized as a parameter for assessing toxicity, there are still certain occasions when some useful information could be obtained from such studies such as giving a clue on the range of doses that could be used in studies like this. These results are consistent with previous studies conducted by some researchers [12,13].

2. Material and methods

2.1. Plant materials

The bark of Persea americana was collected from Jos south area of Plateau state. The plant was identified by a taxonomist with the School of Forestry, Jos, Nigeria. A voucher specimen was deposited at the Department of Pharmacognosy, University of Jos herbarium.

2.2. Extraction and drying of extract

The bark of Persia americana was collected and dried in a shade for two weeks and thereafter pounded to powder in a wooden mortar with pestle. The extract was prepared by maceration of the plant material using chloroform in a conical flask (100 gm of powder in 250 ml of chloroform for both materials separately) and kept at 4 ^{o}C for 72 hours with intermittent shaking. The extract was finally evaporated to powder in a water bath set at 40 ^{o}C to constant weight the residue was found to give 12.8%w/w yield and stored in a refrigerator at 4 ^{o}C until needed for further investigation.

2.3. Animals

Thirty young albino mice all males (23 – 37 kg) obtained from the Animal House Unit of Bingham University, Jos campus, in cages and then acclimatized to laboratory condition for 7 days prior to experiment. These were fed daily with standard animal marsh and water *ad libitum*.

2.4. Measurement of blood glucose concentration

The blood glucose meter (a biosensor gadget) used in this research was the Ames glucometer GX (model 5421 serial no: 1167411 manufactured by Miles Incorporated Diagnostic Division – Elkhart Indiana 46515, USA). This equipment uses dextrostix reagent strips (for measurement of glucose concentration in blood) manufactured by Bayer Company and distributed by Bayer Diagnostic of 13 Rue Jean Jaules, 92807 Plateau Cedex, and France.

2.5. Procedure for effect of acute administration of the chloroform extract of *P. americana* on BGC of Normoglycaemic mice

The effect of chloroform extract of P. americana on BGC of normoglycaemic mice was studied. Fifteen healthy albino mice (23 – 37 mg) divided into three groups labeled 1 to 111. At the end of 24 hours overnight food fast, animals in the three groups were as outlined below:

- Group 1 – Equi-volume of distilled water
- Group 11 – 1200 mg/kg IP CHE – PA
- Group 111 – 20 mg/kg IP tolbutamide (reference group)

Immediately after treatment, blood glucose concentrations (BGCs) were measured using the glucometer at 0, ½, 1, 2, 4 and 8 hours by nipping off the terminal end of the animals' tail and squeezing out a drop (second drop) of blood onto the sensor pad of the test strip and inserting it into the glucometer and the blood glucose concentration (BGC) read-off. The relationship between the BGC and time following administration of a single dose of each extract was plotted and compared with that of control and the reference drug tolbutamide.

2.6. Effect of chronic administration of chloroform extract of *P. americana* on the BGC of normoglycaemic mice.

The effects of chronic administration of the chloroform extract of *P. americana* on BGC in normoglycaemic mice was studied. Fifteen (15) young healthy adult male albino mice (31 – 45g) were divided into three (3) groups of five (5) animals each, and labeled groups 1 to 111 Animals were given the extract daily intraperitoneally for twenty-five (25) days as indicated below:

- Group I - Equi-volume of distilled water
- Group II – 400 mg/kg IP CHE- PA
- Group 111 – 10 mg/kg tolbutamide (reference drug)

2.7. Procedure for effect of acute administration of the chloroform extract of *P. americana* on the BGC of STZ – induced hyperglycaemic mice

The procedure is the same as that described in A above except that the animals were previously made hyperglycaemic by administration of 80 mg/kg streptozotocin IP and showed to develop hyperglycaemia within three days before the start of the experiment.

2.8. Procedure for effect of chronic administration of chloroform extract of *P. americana* on the BGC of STZ – induced hyperglycaemic mice.

Again, the procedure used was the same as method adopted in B except that the animals were previously made hyperglycaemic by administration of 80 mg/kg streptozotocin IP before the start of the experiment.

2.9. Statistical analysis of results

Results were expressed as the mean ± standard error of mean (SEM) Statistical analysis of data was carried out using one-way analysis of variance (ANOVA).

3. Results and discussion

Acute administration of the chloroform extract of *P. americana* did not significantly lower the BGC of normoglycaemic animal unlike a single dose of 20 mg/kg IP tolbutamide (reference drug) which significantly lowered the BGC two hours from treatment (*Table 1*).

Table 1 BGC following acute administration of CHE-PA in normoglycemic mice

BGC values (mean ± SEM mg/dL) at different times (hrs.)						
Group Treatment (single dose)	**()**	**½**	**1**	**2**	**4**	**8**
Equi- vol of DW	96±5.2	102 ± 1	97 ± 3.1	91 ± 4.3	88 ± 6.0	93 ± 4.2
1200 mg/Kg IPCHE-PA	92 ± 5.6	94 ± 5.3	87 ± 4.8	89 ± 3.9	93 ± 4.6	89 ± 42
20 mg/Kg Tolbutamide	93 ± 6.3	87 ± 3.7	72 ± 3.7	69 ± 2.7	65 ± 3.1	63 ± 4.7

Chronic administration of the extract in normoglycaemic animals did not significantly alter the BGC when compared to the control and reference drug groups (*Table 2*).

In the STZ – induced hyperglycaemic animals, acute administration of the extract lowered the BGC in a prolonged manner (*Figure 1*).

Table 2 BGC following chronic administration of CHE-PA in normoglycemic mice

BGC Values (mean$\pm$56 mg/dLA) on days						
Group Daily treatment	**1st day**	**5th day**	**10th day**	**15th day**	**20th day**	**25th day**
Equi.vol of DW	82 $\pm$ 3.8	78 $\pm$ 2.4	84 $\pm$ 3.2	83 $\pm$ 4.4	80 $\pm$ 4.8	78 $\pm$ 5.4
400 mg/Kg IPCHE-PA	86 $\pm$ 4.3	76 $\pm$ 5.8	81 $\pm$ 5.5	88 $\pm$ 3.2	91 $\pm$ 5.8	85 $\pm$ 3.9
10 mg/Kg IP Tolbatamide	68 $\pm$ 4.8	65 $\pm$ 2.7	67 $\pm$ 3.7	63 $\pm$ 3.5	65 $\pm$ 4.3	61 $\pm$ 4.3

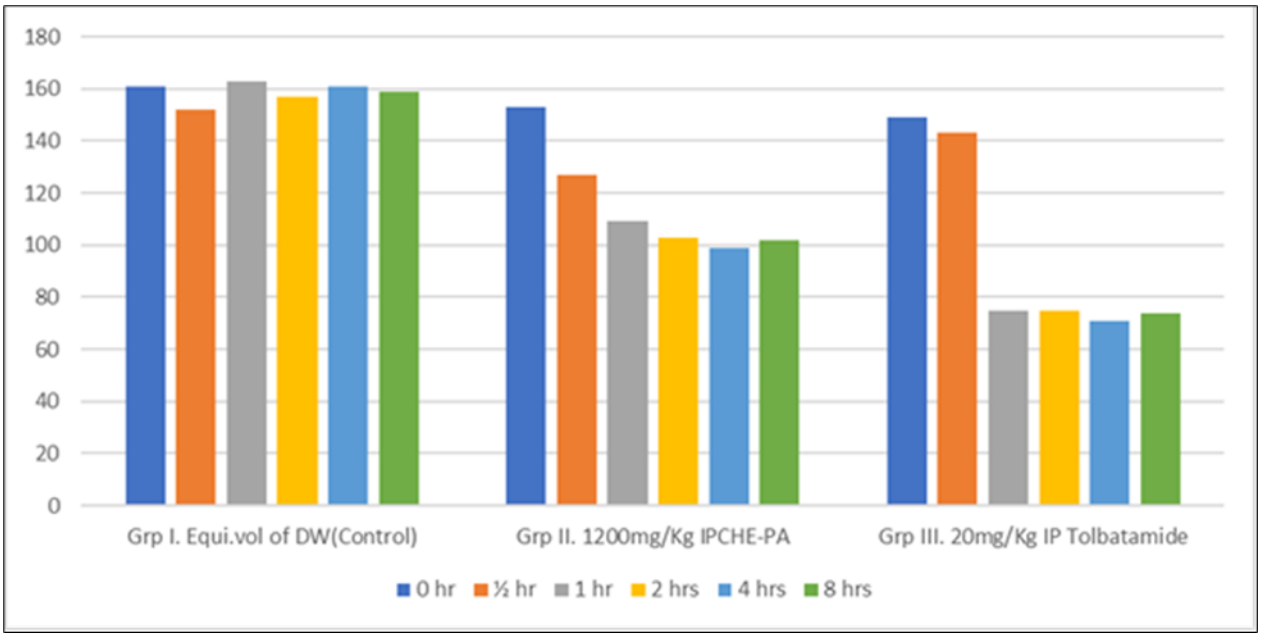

Figure 1 BGC following acute administration of CHE-PA in STZ induced hyperglycaemic mice

Chronic administration of the extract to STZ – induced hyperglycaemic animals showed sustained lowering of BGC compared to the control animals and this compared with the reference drug tolbutamide (*Figure 2*).

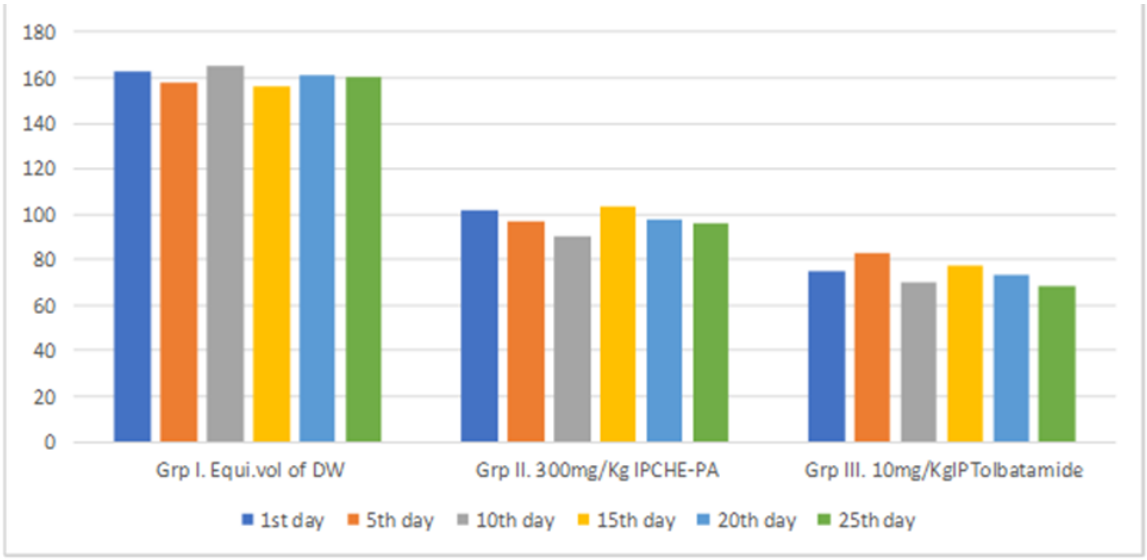

Figure 2 BGC following chronic admin. of CHE-PA in STZ induced hyperglycaemic mice

It can be observed from the studies that acute and chronic administration of the chloroform extract of *P. americana* on normoglycaemic animal did not significantly reduce the BGC unlike a single dose of 20mg/kg IP tolbutamide (reference drug) which significantly lowered the BGC two hours after treatment. In the STZ – induced hyperglycaemic animals, acute and chronic administration of the chloroform extract of *P. americana* showed sustained drop of BGC compared to the control animals and this compared with the reference drug tolbutamide.

4. Conclusion

These results suggest that chloroform extract of *P. americana* produced significant reduction of blood glucose concentration when used acutely and chronically in mice. However, this study suggests for future work the detailed toxic and pharmacological effects of the extracts of *P. Americana.*

Compliance with ethical standards

Acknowledgments

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Disclosure of conflict of interest

Authors hereby declare no conflict of interest.

Statement of ethical approval

Ethical standard was maintained according to required best practices. Two of the authors and Mrs L Kamoh are licensed to handle Laboratory animals and carry out Laboratory procedures involving Laboratory animals.

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