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Original Research Article

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## Preliminary comparative effect of the aqueous extract of *Persea americana* seeds on the blood pressure of normotensive rabbits and rats

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### Abstract

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**Purpose:** Different parts of *Persea americana* are widely used in ethno-medicine to treat and manage various ailments such as epilepsy, febrile convulsion and hypertension. The aim of this study was to comparatively evaluate the blood pressure lowering effect of aqueous seed extract of *Persea americana* on rabbits and rats at different graded doses and to assess the influence of species variation on dosage tolerance.

**Methods:** The animals were prepared for blood pressure evaluation following well established protocol. Comparatively, blood pressure evaluation was carried out in normotensive rabbits and rats, at the dose range of 0.625-5.0 mg/kg and 0.625-2.5 mg respectively.

**Results:** The extract caused a dose dependent (0.625 - 5.0 mg/kg) fall in the systolic, diastolic and mean arterial pressure in both rabbits and rats blood pressure. The extract significantly reduced the mean arterial blood pressure from the basal level of  $112.5 \pm 9.35$  to  $69.86 \pm 10.15$  mmHg at the dose of 5.0 mg/kg in the rabbits and from the basal of  $95.65 \pm 10.33$  mmHg means arterial pressure to  $43.1 \pm 11.15$  mmHg in the rats at the dose of 2.5 mg/kg ( $p < 0.01$ ).

**Conclusion:** The results of the study showed that extract of *Persea americana* has blood pressure lowering effect in the rodent species evaluated, possibly with a narrow therapeutic margin.

**Keywords:** *Persea americana*, normotensive, rat, rabbit, effective dose

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### Introduction

A modest increase in blood pressure above the optimal values (<120/80 mmHg) predisposes an individual to developing hypertension and target organ damage [1]. Despite the enormous investment in the research and development of orthodox drugs for the treatment of hypertension and other cardiovascular diseases, the cure for hypertension hitherto seems to be unattainable, causing a serious need for worry because sometimes elevated blood pressure could become refractory to treatment.

The many claims of traditional/alternative medicine practitioners about the curative powers

of herbs on many disease conditions, including hypertension have attracted attention from researchers, generating renewed interest in the need to exploit the potentials of this natural source of valuable drugs. It is a well-known fact that plants have provided secondary metabolites that have been utilized as chemical models or template for the design and synthesis of orthodox drugs. Clinically useful drugs that cut across all health challenges have been discovered from plants. For instance, artemisinin was isolated from a Chinese plant, *Artemisia annua*, and from this came other derivatives like dihydroartemisinin, arthemeter and artesunate which are more potent than the parent drug [2]. Reserpine is one of the components of the

antihypertensive formulation called “brinerdin”. Reserpine was isolated from *Rawoulfia serpentina*, an India medicinal plant. In spite of the endless list of plant based drugs; there are still many plants that have the potential of being directly useful in the management of diseases and also likely to provide valuable leads to the design and synthesis of new potent drugs, especially in cardiovascular diseases.

*Persea americana* has been used in ethno medicine to treat diseases that cut across all health problems. The seed of *Persea americana* cut into pieces, dried and pulverized is given to individuals to overcome diarrhoea and dysentery, while the oil extracted from the seed is applied to heal skin eruption [3]. Pharmacological screening has shown that the leaves of *Persea americana* is effective in the management of convulsion [4], diabetes and high level cholesterol [5] and as an analgesic and anti-inflammatory agent [6].

The blood pressure lowering effect of *Persea americana* has also been reported. Anaka et al reported the blood pressure lowering effect of the *Persea americana* at the doses of 240, 260 and 280 mg/kg [7]. Imafidon and Amaechina also reported the hypotensive and antihypertensive effects of the aqueous seed extract of *Persea americana* at the doses of 200, 500 and 700 mg/kg respectively administered orally, mixed with animal feeds to rats [8].

There are also documented evidence of the toxicity of *Persea americana* to some animal species. It has been reported that cats, dogs, rabbits, rats, birds, fish and horses can be severely harmed or even killed when they consume the leaves, bark, skin or pit of *Persea americana* [9]. Oelrichs reported that *Persea americana* leaves contain a toxic fatty acid derivative known as persin which, when ingested in sufficient quantity can cause equine colic, which could lead to death in the absence of prompt veterinary treatment [10].

This study reports the preliminary comparative screening of the aqueous extract of the seed of *Persea americana* in normotensive rats and rabbits, and to evaluate the influence of species variation in the dosage tolerability and response to the extract of *Persea americana*.

## Methods

### Materials

Albino wistar rats and rabbits, urethane anaesthetic (Sigma Aldrich Germany), 23 G scalp vein canula (Dana Pharma, Nigeria) and atropine sulfate (Sigma Aldrich Germany), unichannel recorder model 7050 (Ugo Basile, Italy) and normal saline (Unique Pharmaceuticals, Nigeria).

### Plant material and extraction

The fresh fruits of *Persea americana* were obtained from Benin City. The seeds of *Persea americana* were collected as fresh fruits, rinsed thoroughly in clean water, chopped into small pieces and sun dried for twenty (20) days. The dried pieces of the seeds were pounded in a mortar until smooth and then sieved to obtain fine powdered particles. The powdered material was extracted with hot distilled water maceration for 60 min and filtered with cotton wool. The filtrate was concentrated in a rotary evaporator at 70 °C to obtain a semi solid which was dried in an oven at 40 °C. The specific weight of the extract was dissolved in an appropriate volume of physiological saline, to obtain a stock solution of the desired concentration of 100 mg/ml from which calculated doses were administered to the animals during the experiment.

### Phytochemical screening

Phytochemical screening was carried out on the extract following previously described methods [11,12].

### Blood pressure experiment

The effect of the extract on blood pressure was evaluated using normotensive rabbits (1.5-2.0 kg) and rats (220-300 g) of either sex. Each animal was anaesthetized with urethane at the dose of 1750 mg/kg intravenously and the protocol for dissection and canulation as described by Amaechina and Omogbai was followed [13]. When all the measurable variables have remained stable, calculated doses of the extract were administered to the rats (0.625-2.5 mg/kg) and rabbits (0.625- 5.0 mg/kg), and the effect on blood pressure were recorded.

**Statistical analysis**

All data were analyzed with Graphpad prism package version 6.0, and presented as mean ± SEM.

**Results**

**Phytochemical screening:**

Phytochemical results showed that the aqueous seed extract of *Pearsea americana* contained saponins, glycosides, cardiac glycosides, tannins, garlic acid, pseudo tannins, bryan-phenols and cyanogenetic glycosides as shown in Table 1.

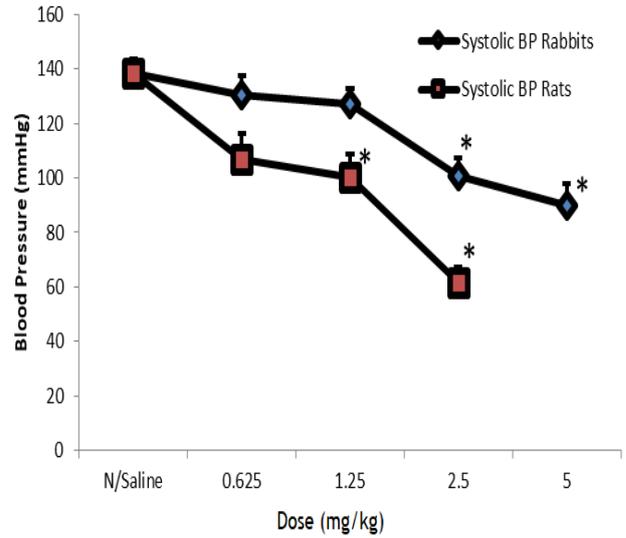
**Table 1:** Phytochemical constituents present in the seeds of *Persea Americana*

Constituents	Results
Saponins	+
Glycosides	+
Cardiac glycosides	+
Tannins	+
Garlic acid	+
Peudo tannins	+
Bryan-phenol	+
Cyanogenetic glycosides	+

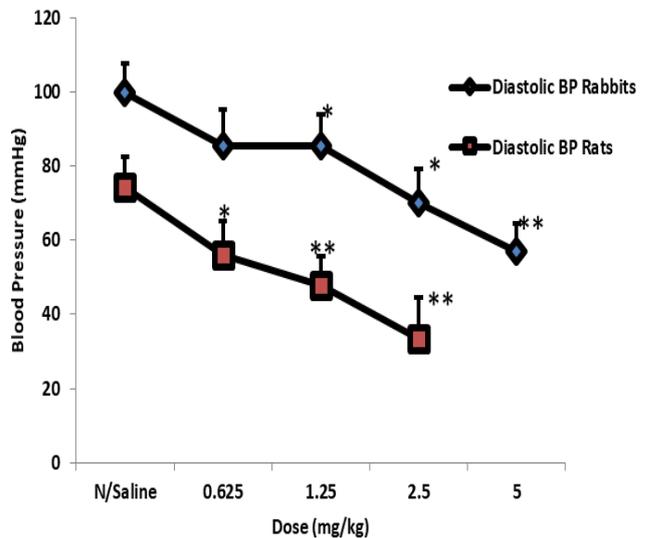
**Blood pressure screening**

The results of the various experiments are presented as mean systolic, diastolic and mean arterial blood pressure plus standard error of the mean. Figures 1, 2 and 3 show the effects of the extract on the systolic, diastolic and mean arterial blood pressures of normotensive rabbits and rats used in the experiments respectively.

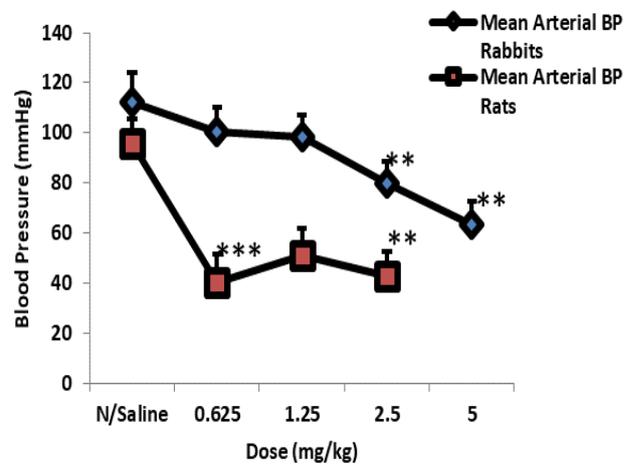
The extract caused a dose dependent fall in the mean systolic, diastolic and mean arterial blood pressure of both the rabbits and the rats respectively. The extract reduced the systolic blood pressure significantly ( $p < 0.01$ ) at the dose of 5 mg/kg from a basal level of  $138.5 \pm 11.25$  to  $89.79 \pm 9.4$  mmHg in the rabbits and from the same basal level of  $138.5 \pm 11.25$  to  $33.4 \pm 7.89$  mmHg at the dose of 2.5 mg/kg ( $p < 0.01$ ). The extract also significantly reduced the mean arterial blood pressure from the basal of  $112.5 \pm 9.35$  to  $67.66 \pm 10.15$  mmHg ( $p < 0.01$ ) in rabbit, and from the basal level of  $95.6 \pm 10.33$  to  $43.1 \pm 11.05$  mmHg ( $p < 0.01$ ) at the doses of 5 mg/kg and 2.5 mg/kg respectively.



**Figure 1:** The effect of extract on the systolic blood pressure of normotensive rabbits and rats.



**Figure 2:** The effect of extract on diastolic blood pressure.



**Figure 3:** The effect of the extract on mean arterial pressure.

## Discussion

Results of this study showed that the aqueous extract of the seed of *Persea americana* has blood pressure lowering effect in a dose dependent manner (0.625-5.0 mg/kg for rabbits) and (0.625-2.5 mg/kg for rats). The blood pressure lowering pattern of the extract revealed a high degree of potency as the dose of 5 mg/kg caused the highest fall in the mean systolic, diastolic and mean arterial pressure of  $89.79 \pm 9.4$ ,  $56.90 \pm 11.9$  and  $67.86 \pm 10.15$  mmHg respectively, and was the highest tolerable dose for rabbits in this study. The maximal effective and tolerable dose of the extract in rats was 2.5 mg/kg, which caused a fall in the mean systolic, diastolic and mean arterial pressure of  $61.5 \pm 10.78$ ,  $33.40 \pm 7.89$  and  $43.10 \pm 11.15$  mmHg respectively.

None of the rodent species survived beyond the maximal effective dose it tolerated during the study. This is suggestive of high potency with narrow therapeutic window following the intravenous administration of the extract of *Persea americana* to the animals used in this experiment. This result tends to agree with the report of Clipsham in avocado pear toxicity [9]. Clipsham reported that animal species are particularly sensitive to various parts of avocado plant and have suffered severe toxicity or even death on ingestion of the avocado plant.

It is important also to note that the result of this comparative study on rabbits and rats is completely at variance with the study reported by Anaka *et al* [7] which reported an effective minimal dose of the aqueous seed extract of *Persea americana* at 248 mg/kg, up to a maximum tolerable dose of 260 mg/kg administered intravenously. Whereas Imafidon and Amaechina also reported effective antihypertensive dose range (200, 500 and 700 mg/kg) respectively of *Persea americana* [8], it should be noted that these doses were administered with animal feeds through the oral route where pharmacokinetic parameters such as first pass effect, tissue binding tend to reduce the bioavailability of most orally administered drugs drastically. However, for intravenously administered drugs, the bioavailability is expected to be 100 %. This singular fact amongst others accounts for the reason why the

intravenous dosing of drugs is usually lower than that of oral routes.

The hypotensive effect of the extract was tilted towards a potentiated toxicity after the administration of by 1.0 mg/kg dose of atropine administered twenty minutes as none of the rodent species used in this study was able to tolerate and survive the earlier mentioned least effective dose of 0.625 mg/kg. This is also suggestive of possible lethal interaction of the active secondary metabolites with muscarinic receptor antagonist.

## Conclusion

The study concluded that the aqueous extract of the seed of *Persea americana* has blood pressure lowering effect in both albino rats and rabbits. The death of the rodent species beyond the dose ranges used in this study is suggestive of a narrow therapeutic window, which therefore calls for caution in the use of the aqueous seed either as direct extract or as decoction in herbal medical practice. The study also concluded that specie difference in rodents does not in any way influence the dosage tolerance to the aqueous extract of the seed of *Persea americana* when administered intravenously.

## Conflict of Interest

We declare that there is no conflict of interest associated with this work.

## Contribution to authorship

The authors declare that this study was carried out by the authors listed in this article, and accept liabilities pertaining to claims thereof. Eboka C and Amaechina FC sourced the plant material. The Pharmacological evaluation was done by Amaechina FC, Oboh C, Uchendu PA and Nnamdi A.

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