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Original Article

A Preliminary Comparative Investigation of Hypotensive Activities of Ethanolic Extracts of *Securidaca Longepedunculata, Olax Subscorpioidea and Persea Americana* on Albino Rats

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Abstract

Background and Aim: *Securidaca longipedunculata, Olax subscorpioidea* and *Persea americana* are medicinal plants that serve several purposes in treating many ailments. In this study, the cardiovascular activities of ethanolic extract of the plants were separately assessed using rats of average weight of 181g.

Materials and Methods: Twenty rats were utilized for each plant. Cardiovascular parameters were recorded through cannulation of the carotid artery on anaesthetized normotensive rats, following the intravenous administration of the ethanolic extract of *S. longepedunculata* (50-200mg kg^{-1}), *O. subscorpioidea* (12.5 -50mg kg^{-1}) and *P. americana* (200 and 400mg kg^{-1}). Acetylcholine and nifedipine served as reference drugs while 0.9% saline was the control. After the administration of the extracts, the physiological reactions of the animals were recorded via a polygraph device fastened to a pressure transducer.

Results: The elicited extract significantly ($p<0.05$) decreased pulse rate, mean arterial, and systolic as well as diastolic blood pressure. These extracts produced significant blood pressure variation patterns, suggesting increased hypotensive activities. This may be adduced to the likely presence of some phytochemicals such as flavonoids in the plants that could possibly act as vasodilators or inhibitors of angiotensin converting enzymes. It may act like calcium channel blockers, β-blockers or natriuretic peptides.

Conclusion: This pharmacological investigation; therefore, gives credence and justification to the ethnomedical, anecdotal and folkloric uses of *S. longepedunculata, O. subscorpioidea* and *P. americana* as blood depressants and it was revealed that *O. subscorpioidea* is more potent followed by *S. longepedunculata* and *P. americana* being the least potent one.

Keywords: *S longepedunculata, O. subscorpioidea, P.* Diastolic blood pressure, Hypotensive, Mean arterial blood pressure, Pulse rate

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Introduction

Hypertension is a major cardiovascular disorder rampant in developed and developing countries, reportedly being a leading cause of morbidity and mortality globally, afflicting almost 72 million people in the United States and more than one billion people worldwide (1). The burden of hypertension is reported

to be greatest in low-income and middle-aged countries characterized by infection frequency of 1 in every 5 adult (2). Moreover, approximately 13.4 million Nigerians of 15 years old and above are reported to be hypertensive, implying that hypertension is 11.2% prevalent among male and female Nigerians (3).

Medicinal plants have traditionally been regarded as efficient sources of medicine for curing various diseases and ailments. The importance of medicinal plants in the management of diseases and as a source for new drugs can never be overemphasized (4). They are easily accessible, cheap and elicit relatively low side effects, thereby giving credence to their wide acceptability (3). *Securidaca longipedunculata* Fresen (family Polygalaceae) is a semi-deciduous shrub commonly called violet tree. *S. longepedunculata* has long been used in herbal medicine in most African countries (5). *Olax subscorpioidea (Oliv*), family Olacaceae, has been traditionally used in the treatment of various ailments such as constipation (6), management of cancer (7) and rheumatism (8). Preliminary phytochemical studies have shown that its stem contains alkaloids, flavonoids, and steroids (9), and the root contains glycosides, alkaloids, steroids and terpenoids (10). Reported pharmacological significance of *P. americana* includes analgesic, anti-inflammatory and vasorelaxant activities (11). Different parts of the plant have been utilized in one medicinal value or the other (12). Many plant extracts are potent due to the presence of different metabolites or phytochemicals usually found in various parts like leaves, bark, roots and fruits thus presenting them as drugs in pharmaceutical industries for the preparation of synthetic medicines (12). The paucity of ethnomedical and pharmacological information on *S. longepedunculata*, *O. subscopioidea* and *P. americana* activities on blood pressure parameters prompted us to investigate its cardiovascular activities on rats.

Materials and Methods

Collection and Authentication of Plant Materials

The plants used for this study, *Securidaca longipedunculata* (root bark), *Olax subcorpioidea* (leaves) and *Persea americana* (leaves) were obtained from Ibadan, Oyo State, Nigeria in February, 2019. *S. longipedunculata* and *O. subcorpioidea* were identified and authenticated in Forestry Research Institute of Nigeria (FRIN), Moore Plantation, Oyo State, with Identification Voucher NO. FHI 103049 and FHI 107986 respectively; while *P.* americana was identified in the herbarium of the Department of Botany, University of Lagos, with voucher number, 7457. The research project was approved by the ethical committee in College of Medicine of the University of Lagos with approval number "CMUL/ACUREC/03/21/830".

Preparation of Plant Extracts

565.00g of pulverized leaves of *P. americana*, 785.50g of powdered *S. longepedunculata* and 784.50g of powdered leaves of *O. subscorpioidea* were separately soaked in 2000ml of ethanol for 96 hours, after which they were evaporated using a regulated hot plate at a constant temperature of 40ºC ±1. The crude extraction yielded 35.50g, 72.80g and 171.60g respectively. The crude extracts were then kept at -20 ºC in sterile universal bottles.

Animal Stock

25 Albino rats weighing between 160 and 180 were randomly selected and purchased from the animal house of College of Medicine, Lagos University Teaching Hospital for this study.

Pharmacological Experiments

Effects on Blood

Each rat was anaesthetized with 2ml of sodium pentarbarbitone intraperitoneally. A forcep was used to grab a sizeable portion of the neck, and then a slit was carefully made on the neck by slight incision with a pair of scissors. The narrow slit was further widened using a pair of scissors until the blood vessels of the neck region became visible enough for cannulation. Afterwards, we isolated the femoral vein and carotid artery and cannulated them in order to administer the drug (extract and reference drug) and also to record blood pressure parameters, respectively. The cannulae were filled with heparinized saline to prevent clotting. We recorded blood pressure using a pressure transducer on a Grass polygraph. Varying doses were selected based on trials for each plant that did not cause lethality but effective (50, 100, 200mg kg^{-1} for *S.longipedunculata*, 12.5, 25, 50mg kg^{-1} for *O. subcorpioidea* and 200, 400mg kg^{-1} for *P.*

americana). The standard drug (acetylcholine), saline solution (0.9% saline) and anticoagulant (heparin) were introduced into the animal through the vein.

Statistical Analysis

We used student's t-test was for statistical analysis, and the results were expressed as Mean±SEM. The results were considered significant when $p \leq 0.05$.

Results and Discussion

In table 1, *S. longepedunculata* showed graded dose lowering activities on both the systolic and diastolic blood pressures, and also on mean arterial pressures, with a greater blood pressure lowering effect on the systolic than on the diastolic blood pressure. The effect was significant at 50 mg kg^{-1} for the systolic blood pressure, and mean arterial pressure respectively but at 100mg kg^{-1} for diastolic blood pressure.

In Table 2, treatment exhibited dose-dependent significant decrease across the doses in the systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial blood pressure (MABP), compared to the control. The heart rate (HR) reduced dose-dependently across the doses, though insignificantly, when compared to the control.

In Table 3, the administration of the plant extract revealed effective hypotensive activity. The level of systolic blood pressure (SBP), diastolic blood pressure (DBP), main arterial blood pressure (MABP) and heart rate (HR) reduced significantly in the tested groups and they compared favourably with the standard drug (Nifedipin). The 400mg/kg treatment displayed increased heart rate.

Polygraphs

Plates 1A –D showed the samples of polygraphs recorded during treatment administration and blood pressure activities of the control, 100mg kg^{-1} *S. longepedunculata*, 12.5mg kg^{-1} *O. subscorpioidea* and 200mg kg^{-1} *P. americana* respectively.

In this study, the pulse rate, mean arterial pressure, and systolic as well as diastolic blood pressure significantly reduced; thereby indicating the modulatory effects of the ethanolic extract of *S. longepedungulata, O. subscorpioidea* and *P. americana* on cardiovascular parameters in rats. The resultant hypotension following the administration of extracts on normotensive rats was dose-dependent with the highest effect manifesting with the highest dose. The mechanism of action has not been investigated. However, the presence of metabolites such as flavonoids, saponins, tannins cardiac glycosides, anthraquinones , alkaloids and reducing sugars have been reported in *S. longepedunculata* (13). Moreover, the phytochemical analysis of *Olax subscorpioidea* extract has shown the presence of flavonoids, anthraquinones, saponins, tannins, phlobatannnins, steroids, cardiac glycoside and

Table 1: Activities of *S. longepedunculata* on blood pressure parameters.

Treatment	Pulse rate	MAP	DBP	SBP
Control (saline)	379.20 ± 8.70	106.60 ± 6.30	58.40 ± 2.90	99.80 ± 5.10
50mg kg^{-1}	288.00 ± 48.80^{a}	64.40 ± 2.40^{a}	53.80 ± 4.50	56.40 ± 2.70^{b}
100mg kg^{-1}	172.80 ± 2.90^{b}	55.60 ± 2.40^{c}	49.00 ± 2.20^{b}	48.00 ± 32.00^{c}
200mg kg^{-1}	92.00 ± 8.80^{c}	49.60 ± 3.20^{c}	21.60 ± 1.50 ^{a}	39.80 ± 1.80^{c}
ACH	139.20 ± 11.40^{b}	53.80 ± 4.50^{c}	28.80 ± 3.80 ^{a}	43.80 ± 3.60^{c}

Values are expressed as Mean ± SEM (n=5). $^{a}p<0.05$; $^{b}p<0.01$; $^{c}p<0.001$

Table 2: Activities of *O. subcorpioidea* on blood pressure parameter.

Treatment	SBP	DBP	MABP	HR
Control (saline)	98.8± 23.50	72.0± 14.50	79.9±17.18	430.60±30.00
12.5mg kg^{-1}	68.12 ± 15.24^{a}	57.25±8.77^{a}	60.85±10.85^{a}	420.00±0.00
25mg kg^{-1}	43.45±5.20^{b}	20.00 ±5.82^{c}	27.80±5.32^{b}	420.00±0.00
50mg kg^{-1}	25.10±7.90^{b}	18.00±5.23^{c}	20.33±6.05^{b}	360.00±69.28
Nifedipine	44.20±4.85^{b}	26.60±8.71^{b}	31.73±7.73^{b}	360.00±60.00

Values are expressed as Mean ± SEM (n=5). $^{a}p<0.05$; $^{b}p<0.01$; $^{c}p<0.001$

Table 3: Activities of *P. americana* on blood pressure parameter.

Treatment	SBP	DBP	MABP	HR
CONTROL	82.63±1.68	64.53±1.28	70.53±0.83	390.00±51.96
200mg kg^{-1}	43.13±3.48[a]	32.25±3.97[a]	35.85±3.80[a]	270.00±17.32[a]
400mg kg^{-1}	45.55±1.94[a]	40.13±2.23[a]	42.37±2.41[a]	405.00±15.00[a]
Nifedipine	49.63±2.57[a]	27.83±2.51[b]	35.05±2.54[a]	320.00±14.14[a]

Values are expressed as Mean ± SEM (n=5). [a]p<0.05; [b]p<0.01; [c]p<0.001

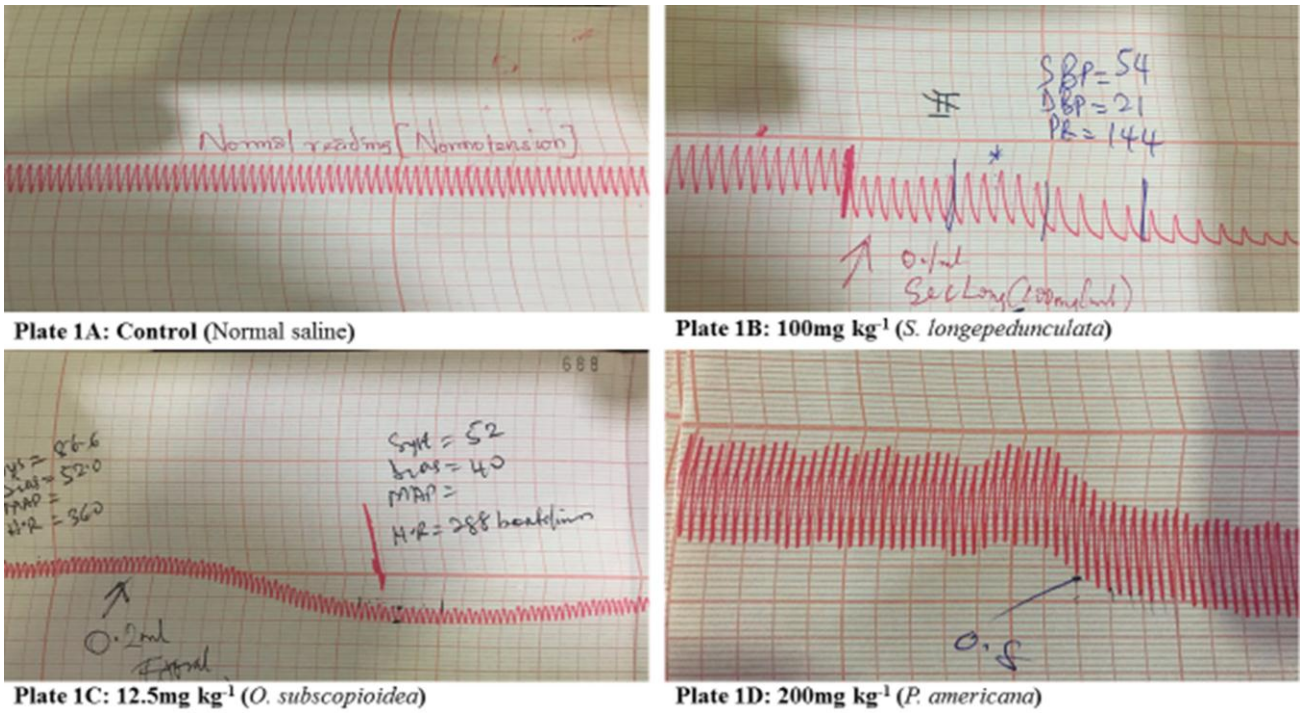

Figure 1. A –D showed the samples of polygraphs recorded during treatment administration and blood pressure activities of the control, 100mg kg^{-1} *S. longepedunculata*, 12.5mg kg^{-1} *O. subscorpioidea* and 200mg kg^{-1} *P. americana* respectively.

polyphenols (9;14). Anaka *et al.*, (15) also reported the availability of flavonoids in *P. americana*. The presence of these effective components may be related to the antihypertensive properties of the extracts. Antihypertensive drugs have been categorized into angiotensin II receptor antagonists, diuretics, b-blocking agents, calcium antagonists, a-receptor blocking agents and angiotensin-converting enzyme inhibitors (1). Flavonoids have been observed to possess tremendous health benefits (16). Flavonoids are composed of a large group of polyphenolic compounds possessing a benzo-γ-pyrone structure and are abundantly found in plants. They are synthesized by phenylpropanoid pathway. According to available reports, the variety of pharmacological activities are caused by secondary metabolites of phenolic nature such as flavonoids for (17, 18). Flavonoids contribute to human protective enzyme systems. The protective impacts of flavonoids against diseases such as cardiovascular diseases and other age-related diseases have been reported in several studies (19, 20, 18). Several mechanisms of action have been proposed through which flavonoids may reduce high blood pressure (16). A typical mechanism of actions of flavonoids include functioning as ACE inhibitors (21). Therefore, *S. longepedunculata* may have acted as ACE inhibitors. Flavonoids in the extracts may have contributed to the hypotensive activity, in consonance with findings of Villar *et al.* (22) where biflavonoids induced endothelium-dependent relaxation. Since the activities of *P. americana* and *O. subscorpioidea* extract were

dose-dependent and compared favourably with the standard drug (Nifedipine), it may have possibly followed a similar mechanism of action of the standard drug. Nifedipine is a calcium channel (23). Even though nifedipine and other dihydropyridines are widely considered as specific to the L-type calcium channel, they also have nonspecific activity with regard to other voltage-dependent calcium channels (24). Nifedipine has long acted as an antagonist of the mineral corticoid receptor, or as an anti-mineral corticoids (25). Hence, *P. americana* and *O. subscorpioidea* may have acted specific to L-type calcium channel by inhibiting the transmembrane influx of extracellular calcium ions into myocardial and vascular smooth muscle cells via L-type calcium channels, inducing the dilatation of the principal coronary and systemic arteries and reducing the myocardial contractility, 'a regular mechanism of Nifedipine' (26).

Conclusion

The results of the present study revealed that the hypotensive activities of the plants exhibited a graded sequence of the root of *S. longipedunculata* > *Olax subcorpioidea* (leaves) > *P. americana* (leaves) through the significant reduction of normotension (normal blood pressure) in rats. Further studies are required to elucidate the precise mechanisms of action and probably determine the bioactive agents. It is also pertinent to evaluate their activities on the established elevated blood pressure.

Acknowledgment

None.

Conflict of Interest

The authors declare that they have no conflict of interest.

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