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Evaluation of Antihypertensive Activity of Aqueous-methanol Extract of *Sida ovata* Grown in Kaura Namoda, Zamfara State

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ABSTRACT

The present study aimed at evaluating antihypertensive activity of aqueous-methanol extract of *Sida ovata* on normal saline induced-hypertensive rats. The induced-hypertensive rats were administered 100, 200, 400 and 800 mg/kg doses of extract of *S. ovata* and their Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Mean Arterial Blood Pressure (MABP) and Pulse Pressure (PP)) were monitored for four weeks. The SBP which were 121.25, 127.55, 138.25 and 141.50 mmHg for week 1, 2, 3 and 4 respectively were lowered to almost normal by 100 mg/kg for week 1 and 800 mg/kg for weeks 2, 3 and 4 respectively. DBP were lowered to almost normal level by 400 mg/kg of the extract except for week 4 that utilized 800 mg/kg to achieve similar result. PP required 400 mg/kg to lower it to almost normal except week 1 that achieved similar result with 200 mg/kg. While 100 and 400 mg/kg were required to lower the MABP to almost normal level for week 1 and 2 respectively, 800 mg/kg was required for weeks 3 and 4. The results showed a dose-dependent decrease in blood pressure. Interestingly, extract of *S. ovata* demonstrated hypertensive potency, making it a good therapeutic agent for managing blood pressure related diseases.

Keywords: Albino rats; Aqueous-methanol extract; Diastolic blood pressure; Dose; Induced-hypertensive; Mean arterial blood pressure; 8% normal saline; Pulse pressure; *Sida ovata*; Systolic blood pressure.

1. Introduction

Cardiovascular diseases have ranked highest amongst the leading cause of death worldwide. Regrettably, hypertension is the most common of them all and a major contributor to the pathogenesis of myocardial infarction, stroke and renal diseases [1]. According to World Health Organization (WHO), hypertension is considered as elevated blood pressure levels above 140/90 mmHg. Findings from literature revealed that about 1.4 billion adults of 30-79 years are hypertensive [2],[3]. Hypertension has claimed millions of lives over time due to negligence of people that pay little or no attention to its signs and symptoms. Hypertension is otherwise known as a silent killer, having much effect on the low and middle income nations of the world [2],[4],[5]. Notably, hypertension could be associated with symptoms such as heart palpitations, headaches, ringing in ears, catching of breath after exertion, pressure to urinate frequently, fatigue, blurry vision, flushed face, dizziness and nosebleeds [3],[6].

Hypertension is classified into two main types: primary or essential hypertension which constitutes 90-95 % and secondary hypertension that accounts for 5-10 % [7]. The causes of primary or essential hypertension could be traced to several activities, such as, deficiencies of vasodilators, increased sympathetic nervous system activity, inappropriate or increased renin secretion, resulting in increased production of angiotensin-II and aldosterone increased production of sodium-retaining hormones and vasoconstrictors, to genetic predisposition. On the other hand, secondary hypertension is caused by certain diseases such as muscular disorders, renal damage, pheochromocytoma, etc., that affect the kidneys, arteries, heart or endocrine system [8].

Various medicinal plants have been used extensively in the management/treatment of hypertension in almost all the nations of the world [9]. The choice of these naturally occurring plants species over other alternatives is due largely their availability as well as cost-effectiveness when compared to synthesized drugs. Interestingly, the absence of the

usual side-effects associated with synthetic drugs, has doubtlessly give medicinal herbs an edge over other sources of hypertension remedies [3],[7]. The present study focused on evaluating the antihypertensive activity of *Sida ovata* grown in Kaura Namoda, Zamfara state, Nigeria, being a herb commonly used in the locality for the treatment of hypertension and associated cases. The choice of S. *ovata* as the plant of interest in the present study is based on its economic relevance as well as its vast ethno-medicinal importance amongst traditional medicine practitioners in the tropical regions of Africa. *S. ovata* has been used in traditional medicine preparations for the treatment of cardiovascular diseases.

1.1. Study Objectives

The main objective of this study was to evaluate the antihypertensive activity of aqueous-methanol extract of *S. ovata* grown in Kaura Namoda Local Government Area of Zamfara state, Nigeria. The specific objectives of the present study include: (i) to induce hypertension into albino rats using 8 % normal saline, (ii) to evaluate the effect of various doses of aqueous-methanol extract of *S. ovata* on Systolic Blood Pressure of the normal saline-induced hypertensive albino rats for a period of four weeks, (iii) to investigate the effect of various doses of aqueous-methanol extract of *S. ovata* on Diastolic Blood Pressure of the normal saline-induced hypertensive albino rats for a period of four weeks, (iv) to determine the effect of various doses of aqueous-methanol extract of *S. ovata* on Pulse Pressure of the normal saline-induced hypertensive albino rats for a period of four weeks, and (v) to establish the effect of various doses of aqueous-methanol extract of *S. ovata* on Mean Arterial Blood Pressure of the normal saline-induced hypertensive albino rats for a period of four weeks.

2. Materials and Methods

2.1. Plant Materials

S. ovata, the medicinal plant used in the present study was collected from Yankaba village in Kaura Namoda Local Government Council, Zamfara State in April 2024 and processed as detailed in Onoja *et al*. [3].

2.2. Animals Used

A total of twenty-eight (28) albino rats (100-120 g) were used in the present study. The rats were housed in standard cages in Biology Unit of SLT Department, Federal Polytechnic Kaura Namoda. The rats were given a standard diet and tap water for the 7 days acclimatization period. All chemicals that were used in this study were of analytical grade and were not subjected to further purification.

2.3. Preparation of Plant Extract

S. ovata roots were washed under tap water and air dried under laboratory condition. The dried sample was segregated and pulverized by mechanically pounding it, using wooden mortar and pestle. The pulverized sample was extracted using aqueous-method (50:50) described by Saleem *et al*. [10], with minor modifications. In the present study, pulverized *S. ovata* sample (3.0 kg) was extracted with 50 % methanol in water (5 L) by cold maceration. The extract was evaporated under reduced pressure to give concentrated extract. The concentrated extract was dried under laboratory condition.

2.4. Experimental Design

The experimental albino rats were allowed to acclimatize for a period of seven days. At the end of the seven days acclimatization period, the albino rats were randomly assigned into three groups; A (n = 4), B (n = 4) and C (n = 20). Group A received tap water and standard feed only and served as positive control. Hypertension was induced into groups B and C. Group B was neither treated with aqueous-methanol extract from *S. ovata* nor standard drug and served as negative control, while group C was further divided into five sub-groups (n = 4), (C_{sd}, C_{o1}, C_{o2}, C_{03}, and C_{o4}) and was given 8 % normal saline solution. C_{sd} group was administered standard drug while others in group C were treated with aqueous-methanol extract of *S. ovata* for consecutive 28 days. The normal saline-induced hypertensive rats in group C_{o1}, C_{o2}, C_{03}, C_{o4} were given *S. ovata* aqueous-methanol extract orally at a dose of 100, 200, 400 and 800 mg/kg (vol. 0.8–0.9 mL) respectively, once daily for consecutive 28 days. Rats in the three groups were fed on standard diet. Blood pressure and pulse pressure of each of these groups were measured at 0, 7, 14, 21and 28 days using NIBP [9],[10].

2.5. Evaluation of Hypertensive Effect in Normotensive Rats

Group B served as negative control and was given 8 % normal saline without either *S. ovata* extract or standard drug, while group C_{sd} and C_{o1} were treated orally with standard drug and 100 mg/kg of *S. ovata* extract respectively for 28 days. Blood pressure and pulse pressure of each of these groups were measured at 1, 7, 14, 21 and 28th day using NIBP technique [10]. In this study, normotensive albino rats (100–120g) were administered *S. ovata* extract 100 mg/kg (vol. 0.8–0.9 mL) orally followed by a saline flush (0.25 mL). The arterial blood pressure was recorded from the carotid artery via an arterial cannula connected to a research grade blood pressure transducer. The temperature of the albino rats was maintained at 37 °C. The mean arterial blood pressure (MABP) of the albino rats was calculated using equation (1) below:

$$MABP = DBP + {}^{1}/_{3} (SBP - DBP) \quad \ldots(1)$$

Changes in blood pressures were expressed as the percent of control values, obtained immediately before the administration of test substance [10]. The above procedure was repeated for extract concentrations of 200, 400 and 800 mg/kg.

2.6. Statistical Analysis

The data generated from the study were presented as mean ± SEM and were subjected to one-way analysis of variance (ANOVA), and statistical differences between the means were evaluated using New Duncan's Multiple Range Test at $P<0.05$.

3. Results and Discussion

3.1. Systolic Blood Pressure

Figure 1 presents the result of systolic blood pressure (SBP) of the test albino rats determined over a period of four (4) week. The mean SBP of the normal rat taken at week 1 was 118.65 ± 0.4787 mmHg while that of the untreated normal saline-induced hypertensive rat (negative control) was 121.25 ± 1.1845 mmHg. On administration of

standard drug to the normal saline-induced hypertensive rat at week 1, the SBP was lowered to 117.25± 1.6520 mmHg. Treatment of the hypertensive rat with 100 mg/kg aqueous-methanol extract of *S. ovata* within week 1 displayed a result similar to that obtained from the standard drug, as it effectively lowered the SBP from 121.25 ± 1.1845 mmHg to 118.75 mmHg. Similarly, the administration of higher doses of the aqueous-methanol extract of *S. ovata* to the hypertensive rats resulted in corresponding decrease in the SBP of the test rat. ANOVA results revealed that the lowering of the SPB of the normal saline-induced hypertensive rats was not dose-dependent as there was no significant difference ($p > 0.05$) between the effect of the higher doses and the 100 mg/kg dose.

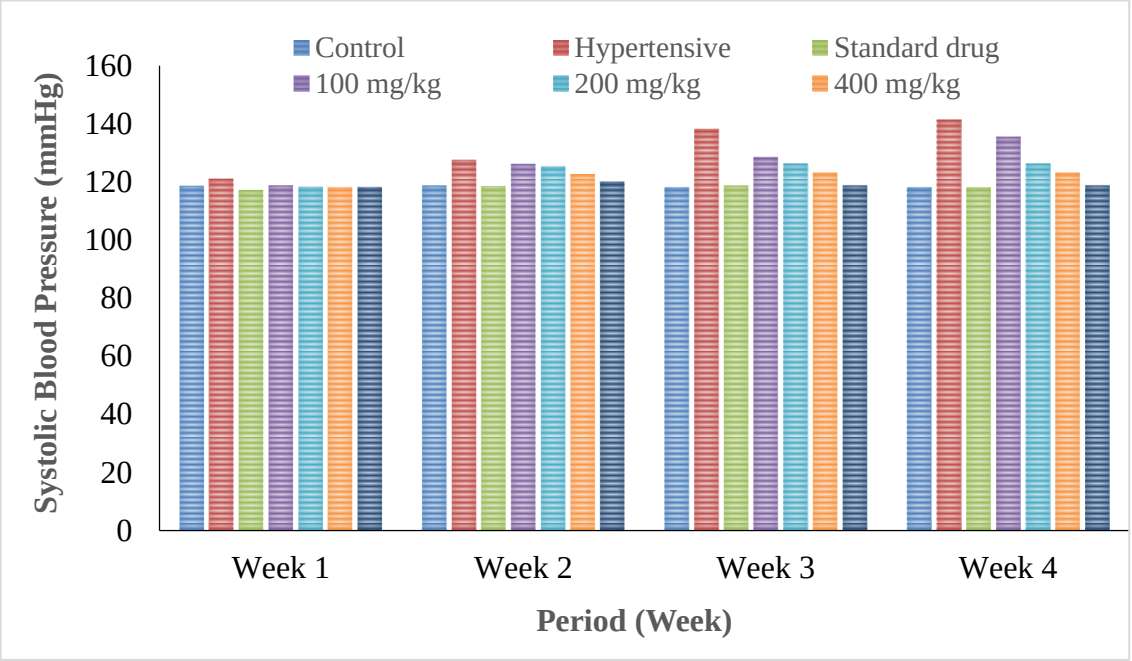

Figure 1. Systolic blood pressure of test albino rats within the four weeks period

At the end of the second week, the SBP of the normal saline-induced hypertensive rat was elevated from 121.25 ± 1.1845 mmHg to 127.55 ± 1.0375 mmHg (Figure 1). Similar to the result obtained in week 1, administration of standard drug to the hypertensive rat effectively lowered the SBP from 127.55±1.0375 mmHg to 118.55±0.9427 mmHg. The aqueous-methanol extract of *S. ovata* demonstrated ability to lower the SBP as observed within week 1. However, the effect of this extract on the SBP at the end of the second week showed a dose-dependent fashion, as there was a corresponding increase in the efficiency of the extract as the dose increases from 100 mg/kg to 800 mg/kg. This is further supported by ANOVA result that indicated a significant difference ($p<0.05$) in the effect of the different doses of *S. ovata* aqueous-methanol extract on the normal saline-induced hypertensive rats.

Interestingly, it was observed that as the experimental period progressed into the 3rd and the 4th weeks, the SBP of the normal saline-induced hypertensive rat increased from 121.25 ± 1.1845 mmHg to 138.25±0.9375 mmHg and 141.50±1.2375 respectively (Figure 1). Administration of both standard drug as well as the various doses of the aqueous-methanol extract of *S. ovata* to the normal saline-induced hypertensive rat demonstrated a trend similar to findings of week 2. Results of both weeks 3 and 4 indicated dose-dependent, as the effectiveness of the extract increased progressively with increase in the dose administered. There was also a significant difference ($p<0.05$) in

the efficiency of the extract as the dose was increased from 100 mg/kg to 800 mg/kg. Findings of the present study corroborated those of Alamgeer *et al.* [9], that evaluated the antihypertensive potential of *Ficus carica* fruit.

3.2. Diastolic Blood Pressure

The results of diastolic blood pressure (DBP) measured for the experimental rats over the period of four weeks are displayed in Figure 2. The DBP of the normative rat was recorded as 79.25±1.0273 mmHg at the end of the first week, while that for the normal saline-induced hypertensive rat was slightly elevated to 82.75±0.5250 mmHg, indicative of the slight hypertension. Administration of standard drug and the various doses of aqueous-methanol extract of *S. ovata* to the 8 % normal saline-induced hypertensive rats resulted in lowering of the SBP to 79.75±1.0085, 81.75±0.3592, 80.75±1.3641, 79.55±1.1472 and 79.55±1.0075 mmHg for standard drug, 100, 200, 400 and 800 mg/kg doses of aqueous-methanol extract of *S. ovata* respectively. The result above clearly showed that the aqueous-methanol extract of *S. ovata* possesses hypertensive potency. However, its effect on DBP revealed a dose-dependent fashion, as the potency increases with increase in the concentration of the extract. Interestingly, ANOVA results indicated a significant difference ($p<0.05$) between 100 mg/kg up to 400 mg/kg, but there was no significant difference in the potency level as the dose was increased from 400 to 800 mg/kg.

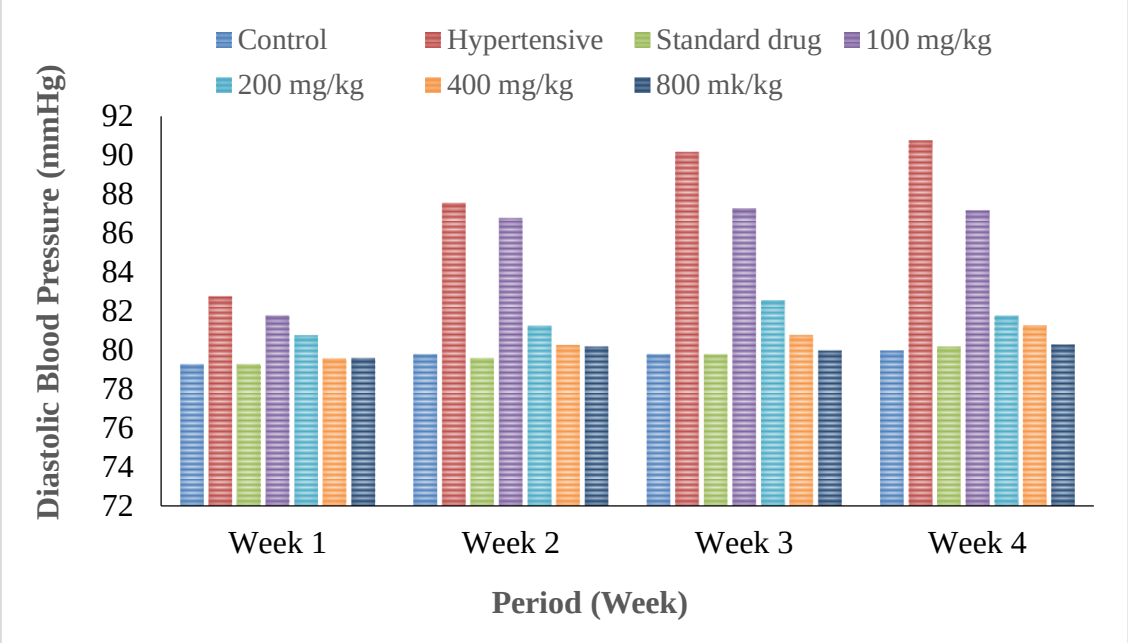

Figure 2. Diastolic blood pressure of test albino rats within the four weeks period

Similar trend in DBP of the experimental rets was observed for weeks 2, 3 and 4 (Figure 2). However, as the weeks went by, the SBP of the experimental rats significantly increased from 87.55±1.1008 mmHg in week 2 to 90.75±1.1052 mmHg in week 4. Within these weeks, the standard drug lowered the SBP of the normal saline-induced hypertensive rats to almost normal. Expectantly, the hypertensive potency of the aqueous-methanol extract of *S. ovata* showed a dose-dependent trend as the potency increased significantly from 100 mg/kg dose to 800 mg/kg dose for all the weeks examined. Correspondingly, it was observed that there was a significant difference ($p<0.05$) in the potency of the extract as its dose was increased from 100 to 400 mg/kg for week 2, but there was no significant difference ($p>0.05$) in the potency of the extract between the 400 and 800 mg/kg doses for

week 2. A slightly different trend was observed for weeks 3 and 4 as there was significant difference ($p<0.05$) between the four different concentrations of the extract administered to 8 % normal saline-induced hypertensive rats. The considerably high hypertensive potency recorded at higher concentrations of the extract is attributed to the available of more active principles responsible for lowering the DBP of the test rats. Findings of the present study are similar to those reported by Alamgeer *et al.* [9].

3.3. Pulse Pressure

The pulse pressure (PP) of the test albino rats were taken for the periods of four weeks and the results are shown in Figure 3. The PP of the normative rat that was 41.05±0.7529 at the beginning of the experiment was raised to 44.95±0.8535, 51.15±1.3520, 48.25±0.9145 and 51.65±0.6525 mmHg at weeks 1, 2, 3 and 4 respectively after inducement with 8 % normal saline. The PP was normalized on treatment with the standard drug. Similarly, administration of various doses of aqueous-methanol extract of *S. ovata* to the 8 % normal saline-induced hypertensive rats effectively lowered their PP in a dose-dependent fashion. Within the first week, there was significant difference ($p<0.05$) in hypertensive potency of the 100 mg/kg and the higher doses. However, no significant difference ($p>0.05$) was observed between the hypertensive potency of the 200, 400 and 800 mg/kg doses of the extract. As the degree of hypertension built up in weeks 2, 3, and 4, the potency of the extract improved with increasing concentration, with 400 mg/kg dose displaying potency similar to the standard drug, for week 2. On the contrary, slightly different results were obtained for weeks 3 and 4, as the extract could not perfectly measure up with the standard drug (Figure 3). This observation suggested that a higher concentration of the aqueous-methanol extract of *S. ovata* would be required to effectively lower the PP of the induced hypertensive rats. Findings of this work is in concordance with existing literature [11].

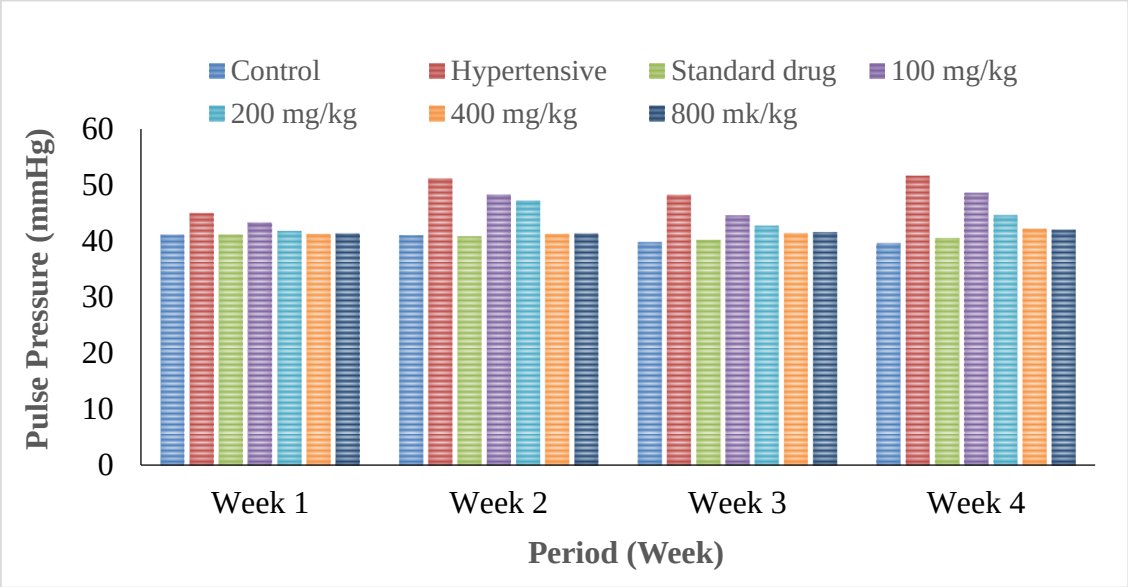

Figure 3. Pulse pressure of test albino rats within the four weeks period

3.4. Mean Arterial Blood Pressure

The results for mean arterial blood pressure (MABP) are shown in Figure 4. It was observed that the value of the MABP of the normative and the 8 % normal saline-induced hypertensive albino rat were 94.15±0.9572 and

98.16 ± 1.1530 mmHg respectively, for week 1. As recorded for the other parameters discussed earlier, administration of the standard drug and 100 mg/kg dose of aqueous-methanol extract of *S. ovata*, resulted in lowering the MABP of the induced hypertensive rat to 94.10±1.0054 and 96.06±0.7561 mmHg respectively. Further raising the dose of the extract to 200 mg/kg resulted in lowering the MABP to 94.75±0.3615 mmHg.

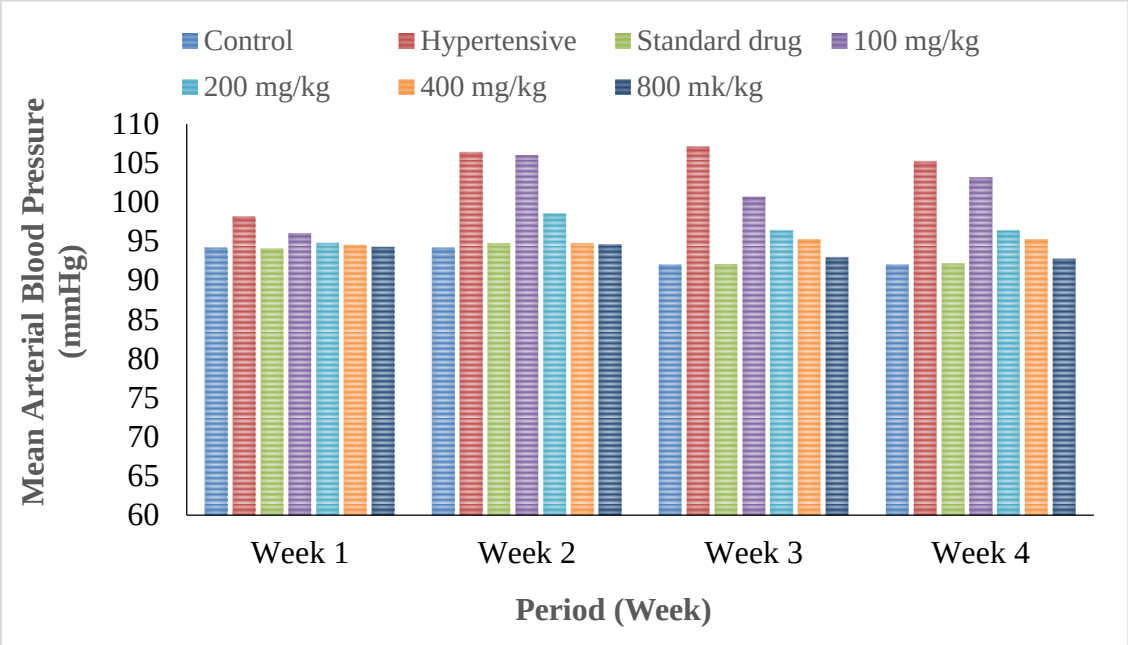

Figure 4. Mean arterial blood pressure of test albino rats within the four weeks period

ANAOVA result indicated that there was no significant difference ($p>0.05$) in the potency level of the extract as the dose was increased from 200 to 800 mg/kg within week 1. This clearly demonstrated that within the first week of induction, the potency of the extract was not dose-dependent. This could be attributed to the low hypertensive level attained within the first week of induction. Interestingly, it was observed that at week 2 of the induction, the MABP level greatly increased from 96.06±0.7561 mmHg in week 1 to 106.32±1.2510 mmHg, and was almost stabilized throughout week 3 and week 4. Administration of 100 mg/kg dose of aqueous-methanol extract of *S. ovata* could not effectively lower the MABP, hence, higher doses of the extract were required to significantly lower the MABP of the induced-hypertensive rats. This observation accounted for the results obtained for week 3 and 4, demonstrating a dose-dependent scenario as there were significant differences ($p<0.05$) between the effects of all the doses administered to the 8 % normal saline-induced hypertensive rats (Figure 4). This observation could be associated with the prolonged effect of the induced hypertension on the rats that has negatively conditioned the MABP to be non-responsive to low concentrations of the extract. Results obtained in the present study closely agreed with those of Saleem *et al.* [10].

4. Conclusion

The study successfully evaluated the antihypertensive activity of aqueous-methanol extract of *S. ovata* root and established that the crude extract had hypertensive potency on the test albino rats as it compared favourably with standard drug. At week 1, SBP of the 8 % normal saline induced-hypertensive albino rats responded to 100 mg/kg dose of the extract. However, as the hypertension prevailed and entered into weeks 2, 3 and 4, higher dose as much

as 400 mg/kg was required to considerably lower the SBP. For DBP, PP and MABP, the most effective dose of the extract was 400 mg/kg for weeks 1 and 2. However, at high hypertensive levels as recorded in weeks 3 and 4, the 800 mg/kg dose was the most effective. It could be concluded from findings of the present study that aqueous-methanol extract of *S. ovata* roots possesses antihypertensive activities, hence justifying its utilization for treatment/management of hypertension amongst the traditional medicine practitioners. The study therefore suggests that 400 – 800 mg/kg crude extract of *S. ovata* is sufficient to manage hypertensive cases.

Additionally, the present study was limited to root extract of *S. ovata* only. Therefore, the study suggested that: (i) antihypertensive activities of the aqueous-methanol extract of the whole plant of *S. ovata* should the explored, (ii) the specific active ingredient of *S. ovata* extract responsible for its hypertensive potency should be isolated and elucidated, (iii) other medicinal efficacy of *S. ovata* plant, other than its antihypertensive activities should be evaluated, and (iv) effect of intravenous administration of the aqueous-methanol extract of *S. ovata* root to the test rats should be investigated.

Declarations

Source of Funding

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Competing Interests Statement

The authors declare no competing financial, professional or personal interests.

Consent for publication

The authors declare that they consented to the publication of this study.

Authors' contributions

All the authors made an equal contribution in the Conception and design of the work, Data collection, Drafting the article, and Critical revision of the article. All the authors have read and approved the final copy of the manuscript.

Availability of data and material

Authors are willing to share data and material according to the relevant needs.

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