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Research Article

# Mitigative Potential of Vernonia amygdalina and Persea americana on Blood Pressure and Urinary Protein in a Rat Model of Preeclampsia

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## Abstract

**Background:** Preeclampsia is a pregnancy-specific hypertensive disorder characterized by elevated blood pressure and proteinuria, often leading to maternal and fetal complications. The search for natural alternatives in its management has led to the evaluation of medicinal plants such as *Vernonia amygdalina* (bitter leaf) and *Persea americana* (avocado). This study aimed to assess the mitigative potential of *Vernonia amygdalina* leaves and *Persea americana* leaves and seeds on blood pressure and urinary protein in a lipopolysaccharide (LPS)-induced rat model of preeclampsia.

**Materials and Methods:** Fifty-four pregnant albino rats were grouped into nine experimental arms (n = 6 per group) and induced with preeclampsia using intraperitoneal injections of 0.1 mL LPS at gestational days 13–14. Treatments were administered for seven days using extracts of *V. amygdalina* (100 and 200 mg/kg), *P. americana* leaf and seed (100 and 200 mg/kg), and Aldoxi (0.036 mg/kg) which is a standard drug. Blood pressure readings and urinalysis for proteinuria were taken before and during induction/treatment. Data were analyzed using one-way ANOVA and Tukey's post hoc test, with statistical significance set at $p \leq 0.05$. Blood pressure, ECG (CODA rat tail cuff system, Kent Scientific) and urinalysis (Dipstick method using metabolic cage) were carried out during/after pregnancy in Cardio Renal unit laboratory, Department of Veterinary Physiology and Biochemistry, Faculty of Veterinary Medicine, University of Ibadan, Oyo state.

**Results:** Prior to inducement, all groups exhibited normal systolic and diastolic blood pressure, and negative proteinuria. Post-inducement results showed significant ($p = 0.03$) increases in systolic (149 mmHg), diastolic (105 mmHg), and mean arterial pressure (120 mmHg) in the negative control (Group B), along with proteinuria. However, all treatment groups demonstrated normalized blood pressure parameters and absence of urinary protein. Rats treated with both *V. amygdalina* and *P. americana* extracts showed physiological and behavioral stability comparable to the standard drug-treated group.

**Conclusion:** The extracts of *V. amygdalina* and *P. americana* (leaf and seed) exhibited promising antihypertensive and anti-proteinuric properties in the LPS-induced preeclampsia rat model. These findings suggest their potential role in the management of preeclampsia and warrant further investigation.

**Kew Words:** preeclampsia; vernonia amygdalina; persea americana; blood pressure; proteinuria; lipopolysaccharide

## Introduction

Preeclampsia is a hypertensive disorder of pregnancy characterized by elevated blood pressure and proteinuria after the 20th week of gestation, posing a significant risk to both maternal and fetal health globally [1]. It is one of the leading causes of maternal and perinatal morbidity and mortality, particularly in low- and middle-income countries, where access to adequate prenatal care is limited [2]. The pathogenesis of preeclampsia is

multifactorial and incompletely understood, involving abnormal placentation, oxidative stress, endothelial dysfunction, and exaggerated inflammatory responses [3].

The current management strategies for preeclampsia largely involve antihypertensive drugs such as labetalol, hydralazine, and methyldopa, alongside close monitoring and, when necessary, early delivery [4]. However, these interventions mainly provide symptomatic relief and are often associated with adverse side effects, high costs, and limited accessibility in resource-constrained settings [5]. This has prompted an increasing interest in exploring natural, plant-based therapies as alternative or adjunct interventions, particularly those with proven antioxidant, anti-inflammatory, and antihypertensive properties.

*Vernonia amygdalina*, commonly known as bitter leaf, is a widely used medicinal plant in African traditional medicine. It contains phytochemicals such as flavonoids, saponins, alkaloids, and phenolic compounds, which have demonstrated potent antioxidant, anti-inflammatory, and hypotensive effects [6]. Previous studies have shown that *Vernonia amygdalina* can ameliorate oxidative stress, reduce blood pressure, and modulate renal function in hypertensive and diabetic animal models [7][8]. These properties make it a promising candidate for addressing some of the pathophysiological hallmarks of preeclampsia.

Similarly, *Persea americana*, commonly known as avocado, is another medicinal plant that has gained attention due to its nutritional and pharmacological value. Its leaves and seeds contain bioactive compounds including flavonoids, tannins, and terpenoids, which have been shown to exhibit antihypertensive, antioxidant, and nephroprotective properties [9][10]. In experimental studies, extracts of *Persea americana* have been found to lower systolic and diastolic blood pressure, reduce proteinuria, and enhance renal and cardiovascular functions [11].

Given the multifaceted pathophysiology of preeclampsia and the limitations of current therapeutic strategies, the exploration of botanical agents such as *Vernonia amygdalina* and *Persea americana* is timely and warranted. These plants possess pharmacologically active compounds that could potentially mitigate the adverse effects of preeclampsia by targeting key mechanisms such as oxidative stress, endothelial dysfunction, and renal impairment. The use of rat models of preeclampsia has become a widely accepted approach to understand the disease mechanism and evaluate potential therapeutic interventions [12]. Induction of preeclampsia in rats' mimics key clinical features such as hypertension and proteinuria, allowing for the investigation of the efficacy and safety of therapeutic agents in a controlled environment [12].

Therefore, this study seeks to evaluate the mitigative potential of *Vernonia amygdalina* and *Persea americana* on blood pressure and urinary protein in a rat model of preeclampsia. The findings from this research may provide a scientific basis for the use of these plants as alternative or complementary interventions in the management of preeclampsia, potentially contributing to improved maternal and fetal outcomes, especially in settings with limited access to conventional pharmacotherapy.

## Materials And Methods

### Collection and Preparation of Plant Materials

Bitter leaves (*Vernonia amygdalina*) and Avocado leaves and seeds (*Persea americana*) were sourced locally in Ikere-Ekiti, Ekiti State, Nigeria. They were identified and authenticated at the Department of Plant Science and Biotechnology, Faculty of Science, Ekiti State University, Ado-Ekiti, Nigeria and assigned the voucher specimen numbers 2022010 and 2022009 for *V. amygdalina* and *P. americana*, respectively. The leaves of the bitter leaf and avocado leaf were detached from the stems. They were rinsed thoroughly with clean water and they were spread on a sack, and placed under room temperature for drying. The drying process took fourteen (14) days, and they were thoroughly observed by turning during this process.

The avocado fruits were cut and opened to remove the avocado seed and grated into smaller pieces for an easy drying process. The grated avocado seed was spread on a sack and placed at room temperature for drying. The drying process took fourteen (14) days, and it was thoroughly observed during this process. The samples were weighed using a weighing balance. It had dried before it was turned into a powder form. The samples (bitter leaf, avocado leaf etc.) were blended using a blending machine and weighed in the laboratory using weighing balance [13].

### Extraction of Samples

The weighed samples were soaked with 95% ethanol for 72 hours in different labelled containers with periodic stirring. After 72 hours, each sample was filtered using the Whatman filter paper and dried. They were preserved at 4 $^{o}$C in the refrigerator for further analysis.

### Experimental Design

Fifty-four female albino rats were obtained from the animal house Faculty of Basic Medical Sciences, College of Medicine, Ekiti State University, Ado Ekiti. They were housed in a plastic cage with steel wire lids, and two male albino rats were introduced into each cage for copulation.

The female albino rat's oestrus cycle was checked in the laboratory after four days using their virginal smear to confirm pregnancy [14]. Few rats were confirmed pregnant on the fourth day and on the sixth day, the entire fifty-four rats were confirmed pregnant, and the male rats were removed from each cage. The pregnant albino rat was then grouped in another cage (Group A to Group I) with six in each cage. The rats were transported to the Cardio Renal Unit Laboratory, Department of Veterinary Physiology and Biochemistry, Faculty of Veterinary Medicine, University of Ibadan, Oyo State, Nigeria.

### Animal Treatment

Lipopolysaccharide (LPS) was used for the induction of preeclampsia at gestational ages 13 and 14 days of pregnancy. Administration of 0.1 mL of LPS through the intraperitoneal route for 3 consecutive days. Treatment was done concurrently with induction but lasted for 7 days. The treatment was as follows:

Group A: Normal control (Feed and water only)

Group B: LPS only

Group C: LPS + 0.036 mg/kg body weight of Aldoxi (a standard antihypertensive drug)

Group D: LPS + 100 mg/kg body of *V. amygdalina* leaf extract

Group E: LPS + 200 mg/kg body of *V. amygdalina* leaf extract

Group F: LPS + 100 mg/kg body of *P. americana* leaf extract

Group G: LPS + 200 mg/kg body of *P. americana* leaf extract

Group H: LPS + 100 mg/kg body of *P. americana* seed extract

Group I: LPS + 200 mg/kg body of *P. americana* seed extract

At the end of the 7-day treatment period, the animals were sacrificed at gestational ages of 20 and 21 days. Blood samples were obtained by cardiac puncture and dispensed into labelled lithium heparin bottles. The blood samples were centrifuged at 4000 rpm for 5 minutes to obtain plasma, which was then stored in sterile plain bottles and refrigerated at -20$^{o}$C until analysis.

### Blood Pressure Determination

The pregnant rats blood pressure was checked and recorded appropriately alongside with the electrocardiograph before and during inducement with treatment. The pregnant albino rats were injected with 0.1ml of ketamine to anaesthetized the rats for electrocardiograph process using ultra sun gel, this enhanced conduction for easy reading of the impulse [15]. Blood pressure, ECG (CODA rat tail cuff system, Kent Scientific) and urinalysis (Dipstick method using metabolic cage) were carried out during/after pregnancy in Cardio Renal unit laboratory, Department Of Veterinary Physiology and Biochemistry, Faculty of Veterinary Medicine, University of Ibadan, Oyo state.

### Urinalysis

The animals were kept in metabolic cage within the space of two hours each before and during urine analysis. Sterile plane universal bottles were used to collect their urine. Urinalysis was done before and during inducement with treatment and also before and during blood pressure determination. The urine collected were analysed using combi 9 stripes.

**Figure 1:** Diagram showing metabolic cage for urinalysis


**Figure 2:** Diagram showing metabolic cage with the animals for urine collection

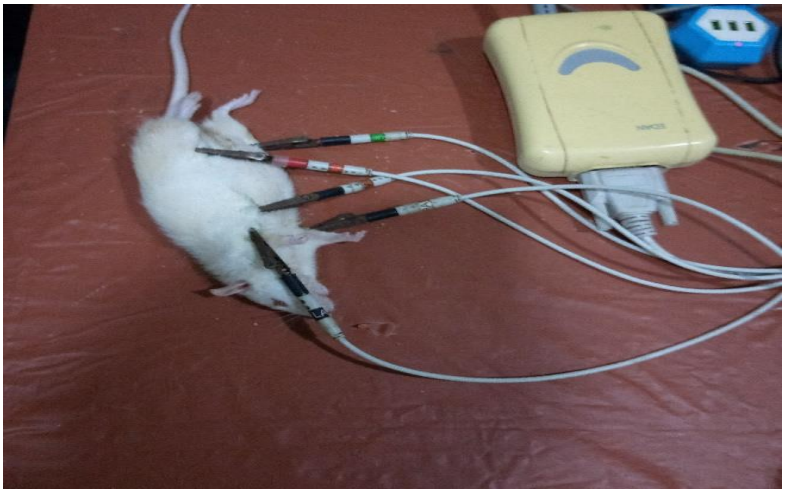

**Figure 3:** A Pregnant Rat undergoing Electrocardiograph

**Figure 4:** A Pregnant Rat undergoing Blood pressure analysis

## Data Analysis

One-way ANOVA was used to analyze the data, and the Tukey post hoc mean comparison test was employed to see whether there were any statistically significant differences between the variables. The analyzed data were expressed as the mean and standard deviation of the mean for six replicates. Statistical significance was defined as a P-value of 0.05 or below ($P \leq 0.05$). GraphPad Prism was used for all statistical analyses (version 8.0).

## Results

As shown in Table 1, all animal groups were healthy and active before pregnancy (Day 1). From Day 2 to Day 12, activeness reduced across all groups, likely due to pregnancy. However, between Days 13 and 16 (after LPS induction and treatment), Group B (LPS only) showed a marked reduction in physical activity and became significantly weak compared to other groups. In contrast, the remaining groups (A, C–I) were less active but remained healthy, indicating some protective or stabilizing effect of the treatments administered.

Before induction, all groups tested negative for protein in urine (Table 2). After five days of treatment, only Group B (LPS only) showed a positive proteinuria result, suggesting kidney dysfunction or preeclampsia-like symptoms induced by LPS. All other groups remained negative, indicating a protective effect of both the standard drug (Group C) and the various plant extracts (Groups D–I).

Blood pressure readings before and after induction are shown in Table 3. Group B exhibited the most significant increase in blood pressure post-induction, with systolic rising from 115 to 149 mmHg, diastolic from 75 to 105 mmHg, and mean arterial pressure (MAP) from 89 to 120 mmHg, confirming a hypertensive state induced by LPS. Other groups (C–I) showed varied levels of improvement or stabilization, with Group C (standard antihypertensive drug) and Groups D–I (treated with plant extracts) maintaining relatively lower post-induction blood pressure values compared to Group B. Group A (normal control) exhibited a slight decrease in all parameters, confirming no induced hypertensive condition.

| **GROUP** | **DAY 1 (**before pregnancy**)** | **Day 2-12** (Pregnant but not induced) | **Day 13-16** (Pregnant, induced with treatment) |
|---|---|---|---|
| **A** | All were healthy and active | Activeness reduced due to pregnancy | Not active but healthy |
| **B** | All were healthy and active | Activeness reduced due to pregnancy | All became so weak compare to others group |

| | | | |
|---|---|---|---|
| **C** | All were healthy and active | Activeness reduced due to pregnancy | Not active but healthy |
| **D** | All were healthy and active | Activeness reduced due to pregnancy | Not active but healthy |
| **E** | All were healthy and active | Activeness reduced due to pregnancy | Not active but healthy |
| **F** | All were healthy and active | Activeness reduced due to pregnancy | Not active but healthy |
| **G** | All were healthy and active | Activeness reduced due to pregnancy | Not active but healthy |
| **H** | All were healthy and active | Activeness reduced due to pregnancy | Not active but healthy |
| **I** | All were healthy and active | Activeness reduced due to pregnancy | Not active but healthy |

**Table 1:** Table showing physiological observation

| Group | Before inducement | After inducement with treatment (After 5 days) |
|---|---|---|
| A | Negative | Negative |
| B | Negative | Positive |
| C | Negative | Negative |
| D | Negative | Negative |
| E | Negative | Negative |
| F | Negative | Negative |
| G | Negative | Negative |
| H | Negative | Negative |
| I | Negative | Negative |

**Table 2:** Table showing Protein urinalysis.

| Group | Systolic | | Diastolic | | Mean Arterial Pressure (MAP) | |
|---|---|---|---|---|---|---|
| | Before inducement | After inducement | Before inducement | After inducement | Before inducement | After inducement |
| **A** | 101 | 91 | 71 | 67 | 79 | 71 |
| **B** | 115 | 149 | 75 | 105 | 89 | 120 |
| **C** | 111 | 110 | 71 | 85 | 83 | 93 |
| **D** | 107 | 104 | 68 | 80 | 86 | 84 |
| **E** | 96 | 101 | 65 | 61 | 77 | 74 |
| **F** | 114 | 110 | 79 | 88 | 85 | 96 |
| **G** | 105 | 114 | 65 | 86 | 80 | 93 |
| **H** | 111 | 105 | 73 | 72 | 83 | 80 |
| **I** | 121 | 103 | 76 | 70 | 91 | 80 |

**Table 3:** Average Blood pressure result before induction and after induction

| Parameter | During pregnancy | Postpartun |
|---|---|---|
| HR (bpm) | 242.94 ± 37.42 | 234.88 ± 33.40 |
| P (sec) | 21.36 ± 7.49 | 26.09 ± 6.79 |
| PR (sec) | 43.94 ± 8.35 | 49.12 ± 7.10 |
| QRS (sec) | 15.7 ± 3.29 | 16.1 ± 2.60 |
| QT (sec) | 79.47 ± 18.45 | 94.63 ± 13.09 |
| QTc (sec) | 157.00 ± 33.56 | 185.23 ±28.86 |
| Ra | 0.33 ± O.15 | 0.39 ± 0.12 |

**Table 4:** Comparison of Electrocardiograph Parameters during Pregnancy and Postpartum

## Discussion

This study aimed to evaluate the ameliorative effects of *Vernonia amygdalina* and *Persea americana* (leaf and seed extracts) on blood pressure and urinary protein levels in a lipopolysaccharide (LPS)-induced rat model of preeclampsia. Across all groups, pregnancy led to a noticeable reduction in activeness. However, Group B (LPS only) displayed the most profound physiological deterioration, becoming weak and less active compared to other groups. This outcome corroborates previous findings that LPS induction mimics systemic inflammation and endothelial dysfunction characteristic of preeclampsia, which affects maternal behavior and mobility in rodents [16]. Interestingly, rats in Groups C through I, particularly those administered *V. amygdalina* and *P. americana* extracts, retained some degree of physical activity despite LPS induction, suggesting a potential anti-inflammatory or protective effect of the treatments. Proteinuria, a hallmark of preeclampsia, was only observed in Group B (LPS-only), indicating successful model induction. All other groups—including the treated groups—did not exhibit protein in urine after LPS induction and subsequent treatment. These findings suggest that *V. amygdalina* and *P. americana* may have renoprotective properties, comparable to the standard antihypertensive (Aldoxi) used in Group C.

This renoprotective effect aligns with earlier studies that reported the nephroprotective potential of *V. amygdalina*, primarily due to its rich flavonoid, alkaloid, and phenolic content, which contribute to oxidative stress modulation [17, 18]. Similarly, *P. americana* has been shown to exhibit antioxidative and anti-inflammatory properties capable of reducing renal oxidative stress and improving kidney function in various animal models [9, 19].

A comparative evaluation of systolic, diastolic, and mean arterial pressure (MAP) values reveals critical insights. Group B showed a significant elevation in all parameters post-LPS induction (Systolic: 149 mmHg; Diastolic: 105 mmHg; MAP: 120 mmHg), affirming the hypertensive state consistent with preeclampsia models [20]. Conversely, treatment with Aldoxi (Group C) normalized blood pressure values, showcasing its efficacy.

Notably, *V. amygdalina* (Groups D and E) at both 100 mg/kg and 200 mg/kg dosages showed a reduction in blood pressure, with the 200 mg/kg dose showing more effective control (Post-induction MAP: 74 mmHg). These findings support previous studies highlighting *V. amygdalina*'s hypotensive activity, attributed to its vasodilatory effects mediated via nitric oxide pathways and calcium channel blockade [21, 22].

Similarly, *P. americana* leaf and seed extracts (Groups F–I) demonstrated considerable antihypertensive potential, with MAP values ranging from 80 to 96 mmHg post-induction. Group I (200 mg/kg seed extract) showed the lowest MAP among *P. americana*-treated groups (MAP: 80 mmHg), closely mirroring normal control values. This suggests that *P. americana* seed extract may have superior antihypertensive effects, possibly due to higher concentrations of bioactive compounds such as phytosterols and polyphenols [11,23]. The comparable efficacy of *P. americana* and *V. amygdalina* to Aldoxi supports the ethnomedical relevance of these plants in managing hypertensive disorders. Their ability to normalize blood pressure while preventing proteinuria implies both vascular and renal protective properties [13,14,15].

The antihypertensive effect of *V. amygdalina* has been extensively validated. Egedigwe et al. [20] demonstrated that aqueous extracts significantly reduced blood pressure in hypertensive rats via antioxidant modulation. This aligns with our findings, especially in Group E, where high-dose *V. amygdalina* reduced MAP to near-normal levels.

Similarly, Adeyemi et al. [9] reported the efficacy of *P. americana* leaf extracts in reducing arterial pressure and improving endothelial function in hypertensive rats. Our results further show that both the leaf and seed extracts are effective, with the seed extract demonstrating slightly superior performance.

Furthermore, in a study by Salami et al. [11], *P. americana* seed extract significantly reduced LPS-induced systemic inflammation, supporting the hypothesis that its bioactive components play a role in modulating endothelial dysfunction—a key driver of preeclampsia. In contrast, the unmitigated rise in MAP and proteinuria in the LPS-only group (B) aligns with previous models where LPS successfully induced preeclampsia-like symptoms, including glomerular endotheliosis and hypertension [16, 24].

## Conclusion

This study presents strong evidence that *Vernonia amygdalina* and *Persea americana*, especially at higher dosages, exert significant antihypertensive and nephroprotective effects in LPS-induced preeclamptic rats. Their efficacy was comparable to a standard drug, underscoring their potential in the management of preeclampsia. These findings lend credence to their use in traditional medicine and provide a foundation for future pharmacological explorations.

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