

## ORIGINAL RESEARCH ARTICLE

# Histological and biochemical effects of *Plectranthus ornatus* extract on the renal system of dexamethasone-induced hypertension in rabbits

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## Abstract

Hypertension is a major public health issue contributing to the global burden of disease and often leading to renal complications. *Plectranthus ornatus* is traditionally used to treat hypertension, despite limited scientific evidence supporting its efficacy. This study investigated the histological and biochemical effects of *Plectranthus ornatus* extract on the renal system of dexamethasone-induced hypertensive rabbits. A total of 20 rabbits were divided into four groups. The negative control group ( $n = 6$ ) received a saline injection; the positive control group ( $n = 6$ ) received a dexamethasone injection; and two dexamethasone-injected groups ( $n = 4$  each) were treated with 200 and 1,000 mg/kg of the extract for a period of 14 days. Histological and biochemical investigations were carried out using standard techniques. Increased systolic and diastolic blood pressure was observed in hypertensive animals induced with dexamethasone (2 mg/kg) in 5% sodium chloride solution. Histological examination showed mild renal inflammation attributable to the high blood pressure. Following extract administration, there was a dose-dependent decrease in blood pressure at both 200 mg/kg and 1,000 mg/kg doses administered by oral gavage. Electrolytes ( $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Cl}^-$ ,  $\text{HCO}_3^-$ ), as well as urea and creatinine levels, remained within acceptable ranges, including in animals administered with the low-dose extract. In addition, the extract produced observable histological changes, particularly at higher doses, without significant impairment of kidney and bladder structure, although these positive changes require further investigation to better understand their implications. These findings suggest that the *Plectranthus ornatus* extract has potential antihypertensive and nephroprotective effects; however, careful optimization of dosage and treatment duration is necessary to minimize adverse effects. Further research is recommended to confirm its long-term safety and efficacy.

**Keywords:** Hypertension; Dexamethasone-induced hypertension; Nephroprotective extract; *Plectranthus ornatus*

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## 1. Introduction

Hypertension is a chronic illness characterized by elevated blood pressure in the arteries. As blood vessel pressure rises, the heart has to work harder to pump blood, causing it to beat more forcefully. It is sometimes called the “silent killer” because there are no obvious symptoms in the early stages.<sup>1</sup> High blood pressure causes about 7.5 million deaths annually, accounting for 12.8% of all fatalities globally.<sup>2</sup> According to Singh *et al.*,<sup>2</sup> the number of adults with hypertension is expected to rise to 1.56 billion by 2025. Patel *et al.*<sup>3</sup> reported that hypertension is present in about 50% of adults between the ages of 60 and 69, and its prevalence increases further after the age of 70.

The percentage of people with high blood pressure (defined as systolic and/or diastolic blood pressure  $\geq$  140/90 mmHg) or uncontrolled hypertension decreased slightly between 1980 and 2010. Nonetheless, over the past decade, significant increases in hypertension cases driven by aging and population growth have been observed across all World Health Organization regions, with Africa experiencing the largest increase of 30%. The Americas had the lowest prevalence of high blood pressure (18%), while the global estimate for adults aged 18 years and older in 2014 was approximately 22%.<sup>4</sup> In Nigeria, hypertension is the most prevalent non-communicable disease. In Nigerian metropolitan hospitals, hypertension and its complications account for over 25% of emergency medical admissions, and it is the most commonly diagnosed cardiovascular condition.<sup>1</sup>

High blood pressure is a significant risk factor for coronary heart disease, stroke, and chronic heart disease. Its complications include heart failure, peripheral vascular disease, renal impairment, retinal hemorrhage, and visual impairment.<sup>2,4</sup> According to Williams<sup>5</sup>, known predisposing factors for hypertension include ethnicity (with Black African and Caribbean patients being more affected), being overweight or obese, physical inactivity, excessive alcohol or salt intake, stress, and comorbid conditions such as diabetes, chronic kidney disease, and sleep apnea. Diwe *et al.*<sup>6</sup> also identified genetic factors and a strong family history as important risk factors. Hypertension is among the most controllable risk factors for cardiovascular disorders. However, in low and middle-income countries (LMICs), there is a substantial lack of knowledge on the management and treatment of hypertension. In addition, competing health challenges such as HIV/AIDS, tuberculosis, and malaria strain health care resources in LMICs, leading to reduced focus on hypertension prevention and control in several LMICs.<sup>4</sup>

One of the major reasons for the high prevalence

of hypertension in sub-Saharan Africa is the transition from traditional to more westernized lifestyles. Although rural communities have historically exhibited lower rates of hypertension and cardiovascular disease risk factors than urban populations, recent data from Sub-Saharan Africa indicate that this gap is narrowing. This trend is attributed to the adoption of modern lifestyles, including smoking, alcohol consumption, high intake of fat, sugar, and salt, low consumption of fruits and vegetables, and sociodemographic changes.<sup>7</sup>

Hypertension, a major risk factor for cardiovascular disease, is primarily managed with conventional antihypertensive drugs such as diuretics, beta-blockers, calcium channel blockers, and angiotensin-converting enzyme inhibitors. However, the limitations of these synthetic drugs, including adverse side effects, high costs, and limited accessibility, have prompted increasing interest in herbal medicine as an alternative treatment option.

Most herbal medicines reduce or control hypertension by exerting antioxidant, anti-inflammatory, and anti-apoptotic effects, stimulating the endothelial nitric oxide synthase–nitric oxide signaling pathway, suppressing endothelial permeability, and promoting angiogenesis. Scientific studies recommend lifestyle modification and the use of appropriate medicinal plants, as many conventional antihypertensive agents are associated with side effects.<sup>8</sup> Approximately 85% of known *Plectranthus* species are reported to possess therapeutic benefits,<sup>9</sup> generating considerable interest in their medical and commercial potential.<sup>10</sup> *Plectranthus* species are widely utilized as food, ornamentals, and medicinal plants in many parts of the world,<sup>11</sup> and are employed by various populations to treat a wide range of ailments.<sup>12</sup> Ethnopharmacological studies have suggested using this herb to manage gastrointestinal disorders.

In certain regions of Brazil, farmers and healers use *Plectranthus ornatus* leaves as an antibiotic for treating skin infections.<sup>13</sup> The use of *P. ornatus* leaves in ethnoveterinary practices has become widespread as a viable alternative treatment due to their safety, low cost, and accessibility. These plants are readily available on small farms and offer a less aggressive approach to animal treatment. Most farmers' practices are based on empirical knowledge and have shown notable success in cattle.<sup>13</sup> In folk medicine, *P. ornatus* is also used to treat dyspepsia and liver failure.<sup>14</sup> *Plectranthus* species contain a variety of bioactive phytoconstituents, including phenolic compounds, monoterpenes, sesquiterpenes, terpenes, and saponins,<sup>15,16</sup> Terpenoids are considered the primary contributors to the biological activities of *Plectranthus* species and are particularly abundant in several members of the Lamiaceae

species.<sup>14</sup> Based on the literature reviewed, there is a lack of scientific studies examining the effects of *P. ornatus* extract on hypertension management and on the histological and biochemical aspects of the renal system. Hence, this pioneering work aims to advance existing knowledge and highlights the potential therapeutic benefits of *P. ornatus* in hypertension and associated organ damage.

## 2. Materials and methods

Twenty healthy New Zealand white rabbits of mixed sex, weighing 500–1,200 g, were used in this study. The animals were monitored at the University of Jos animal farm. They were housed in cages with a wire-mesh flooring and received a pellet diet with water provided *ad libitum*. The animals were divided into four major groups. Hypertension was induced using dexamethasone (2 mg/kg, intraperitoneal injection) combined with 2 ml hypertonic saline (5%) administered orally once daily for five days, followed by 7.5% saline on the sixth day, after which physical signs of hypertension were observed.<sup>17</sup> Ethical clearance was obtained from the Animal Experimental Ethical Committee, Department of Pharmacology, University of Jos (reference: assurance approval-UJ/FPS/F17-00379).

### 2.1. Experimental design

A randomized experimental design was employed, with 20 rabbits divided into four groups (Table 1). The negative control group ( $n = 6$ ) received saline injections, the positive control group ( $n = 6$ ) received dexamethasone injection, and two dexamethasone-injected groups ( $n = 4$  each) were treated with *P. ornatus* extract at doses of 200 and 1,000

**Table 1. An experimental design for evaluating the effects of low and high doses of *Plectranthus ornatus* extract on dexamethasone-induced hypertension in rabbits**

| Group            | Treatment given                                                                    | No. of rabbits |
|------------------|------------------------------------------------------------------------------------|----------------|
| Negative control | Normal saline                                                                      | 6              |
| Positive control | 2 mg/kg dexamethasone injection + 5% NaCl solution                                 | 6              |
| Low dose         | 2 mg/kg dexamethasone injection + 5% NaCl solution + 200 mg/kg <i>P. ornatus</i>   | 4              |
| High dose        | 2 mg/kg dexamethasone injection + 5% NaCl solution + 1,000 mg/kg <i>P. ornatus</i> | 4              |

Note: All groups were assessed for general observations, blood pressure, renal function tests, and renal histology.  
Abbreviation: NaCl: Sodium chloride.

mg/kg body weight for a period of 14 days. The dosage determination and acute toxicity study of *P. ornatus* extract were performed in rats, and the experimental protocols are described in detail in Section 2.3.

After the extract was administered for a period of 14 days, systolic and diastolic blood pressure were measured using standard methods, while biochemical parameters, including blood urea nitrogen, creatinine, and electrolytes (potassium ion [K<sup>+</sup>], sodium ion [Na<sup>+</sup>], chloride ion [Cl<sup>-</sup>], and bicarbonate ion [HCO<sub>3</sub><sup>-</sup>]) were determined using standard methods. The kidney and bladder were also examined histologically through microscopic evaluation.

### 2.2. *Plectranthus ornatus* extraction

The *P. ornatus* plant was collected from Jos North, Plateau State. A voucher specimen was deposited in the Herbarium of the Department of Pharmacognosy and Traditional Medicine, University of Jos, and assigned the voucher number UJ/PCG/HSP/21 L01. To prepare the crude extract, *P. ornatus* leaves were dried in the shade and then pounded into fine powder using a mortar and pestle. A total of 500 g of air-dried, pounded leaves was extracted by cold maceration with 1 L of ethanol in 2.5 L conical flasks, which were tightly covered with aluminum foil and left for 1 week at room temperature. The filtrates were then dried in a fume chamber to ensure complete removal of the extraction solvent.<sup>18</sup> This procedure was carried out at the Pharmacology Department, Faculty of Pharmaceutical Sciences, University of Jos.

### 2.3. Dosage determination

An acute toxicity study was conducted using Lorke's modified method. Twelve 8-week-old Wistar albino rats (XXX), weighing 180–200 g, were used in the study. The animals were housed and monitored at the University of Jos animal farm. In the first phase, nine rats were divided into three groups of three rats per cage. In each group, three rats were orally administered the extract at one of three graded doses (10, 100, and 1,000 mg/kg). In the second phase of the experiment, the remaining three rats were each administered a single oral dose of 1,600, 2,900, and 5,000 mg/kg. The animals were observed closely for the first 4 h for acute behavioral changes, and for a total of 24 h. If mortality occurs, the median lethal dose (LD<sub>50</sub>) is calculated using the formula:

$$LD_{50} = \sqrt{(\text{highest nonlethal dose}) \times (\text{lowest lethal dose})} \quad (1)$$

The LD<sub>50</sub> provided guidance for extrapolating doses used in the experimental phase of the investigation.<sup>19,20</sup>

## 2.4. Hypertension induction and extract administration

All experimental animals were fed with chow for 14 days following an initial seven-day acclimatization period. Hypertension was induced over a period of six days using dexamethasone. At the end of hypertension induction, blood pressure was measured on the 7th and 14th days after treatment initiation and compared across groups.<sup>3</sup>

## 2.5. General physical observations

Animals were observed for changes in eye coloration, fur appearance, alertness, and food and water intake. Body weight was measured before and after treatment to assess the animals' general well-being during the experimental period.

## 2.6. Measurement of blood pressure

After completion of the treatment schedule, an invasive blood pressure measurement was performed. Rabbits from each group were anesthetized with urethane (120 mg/100 g). One of the carotid arteries was cannulated after an incision in the neck region to locate it, and the mean arterial blood pressure was recorded using a manometer. Heparinized saline (0.1 ml/kg) was introduced into the fine polyethylene catheter cannulated into the carotid artery to prevent clotting. Mean arterial blood pressure was determined by observing the highest and the lowest points of the waveform for systolic and diastolic readings, respectively.<sup>3</sup>

## 2.7. Biochemical analysis

Blood samples were collected, and the separated serum samples were used to assess renal function by measuring urea and creatinine levels. These levels were measured using an automated biochemical analyzer (Cobas c111; F. Hoffmann-La Roche Ltd., Switzerland) at the Plateau State Specialist Hospital. Urea and creatinine values were expressed in mmol/L and  $\mu\text{mol/L}$ , respectively, while electrolyte concentrations were expressed in mmol/L.<sup>21</sup>

## 2.8. Histological analysis

The kidneys and bladder were harvested from rabbits in both experimental and control groups at the end of acclimatization, immediately after hypertension induction, and on the 7th and 14th days after treatment with *P. ornatus*. The experimental group that received *P. ornatus* extract treatment was observed for signs of toxicity.

The organs were fixed in 10% formalin and processed to obtain 4  $\mu\text{m}$ -thick paraffin sections using a microtome (MICROM HM 340E, Epreidia, United States of America

[USA]). Sections were stained for histological examination using hematoxylin and eosin.<sup>22,23</sup> This procedure was carried out at Jos University Teaching Hospital.

## 2.9. Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics version 16.0 (IBM Corp., USA) to evaluate renal profile parameters and systolic and diastolic blood pressure outcomes. The data are descriptive only and are reported as mean values without *p*-values. No statistical analyses were performed to compare groups with respect to biochemical parameters or blood pressure profiles.

## 3. Results

The effect of *P. ornatus* on body weights, fur appearance, alertness, eye coloration, and food intake in dexamethasone-induced hypertensive rabbits is presented in Table 2. The weight of the animals increased proportionately with age, feeding, and water intake. However, fur roughness was observed in rabbits on days 7 and 14 after treatment with either the low- or high-dose *P. ornatus* extract.

There was an increase in systolic and diastolic pressure in the positive control. However, there was a reduction in the blood pressure in animals administered with the extract at day 7 as compared to day 14. Hence, we concluded that the extract decreased systolic and diastolic pressures at day 7.

Treatment with *P. ornatus* at a low dose (200 mg/kg) resulted in a slight reduction in both systolic and diastolic readings, although the diastolic readings remained slightly higher than those of the positive control on the same day. At the high dose (1,000 mg/kg), reductions in both systolic and diastolic readings were observed. Notably, the low-dose treatment on day 14 reduced systolic and diastolic values and appeared more potent than the high dose over a longer duration (Figure 1).

### 3.1. Effect of low-dose *Plectranthus ornatus* extract on urea and electrolytes ( $\text{Na}^+$ , $\text{K}^+$ , $\text{Cl}^-$ , $\text{HCO}_3^-$ ) levels

Urea and serum electrolytes ( $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Cl}^-$ , and  $\text{HCO}_3^-$ ) showed little change over time among groups, including groups administered with low-dose extract, and all values were within the normal reference range (normal control; Figure 2).

### 3.2. Effect of high-dose *Plectranthus ornatus* extract on urea and electrolytes ( $\text{Na}^+$ , $\text{K}^+$ , $\text{Cl}^-$ , $\text{HCO}_3^-$ ) levels

Urea and serum electrolytes ( $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Cl}^-$ , and  $\text{HCO}_3^-$ ) showed little change over time among groups, including those administered with high-dose extract, and all values

**Table 2. General observations of the experimental animals under different treatment groups**

| Animals grouping | Body weight (g) | Food intake (g) | Water intake (ml) | Fur appearance | Eye coloration | Alertness |
|------------------|-----------------|-----------------|-------------------|----------------|----------------|-----------|
| Day 1            |                 |                 |                   |                |                |           |
| Negative control | 500             | 359             | 750               | Smooth         | Normal         | Yes       |
| Positive control | 994             | 357             | 749               | Smooth         | Normal         | Yes       |
| LD (200 mg/kg)   | 953             | 359             | 751               | Smooth         | Normal         | Yes       |
| HD (1,000 mg/kg) | 805             | 360             | 752               | Smooth         | Normal         | Yes       |
| Day 7            |                 |                 |                   |                |                |           |
| Negative control | 666             | 717             | 1,200             | Smooth         | Normal         | Yes       |
| Positive control | 1,050           | 714             | 1,498             | Smooth         | Normal         | Yes       |
| LD (200 mg/kg)   | 1,054           | 718             | 1,502             | Rough          | Normal         | Yes       |
| HD (1,000 mg/kg) | 841             | 720             | 1,504             | Rough          | Normal         | Yes       |
| Day 14           |                 |                 |                   |                |                |           |
| Negative control | 768             | 1,076           | 2,250             | Smooth         | Normal         | Yes       |
| Positive control | 1,323           | 1,071           | 2,247             | Smooth         | Normal         | Yes       |
| LD (200 mg/kg)   | 1,129           | 1,077           | 2,253             | Rough          | Normal         | Yes       |
| HD (1,000 mg/kg) | 1,066           | 1,440           | 2,256             | Rough          | Normal         | Yes       |

Abbreviations: HD: High dose; LD: Low dose.

were within normal reference range (normal control; [Figure 3](#)).

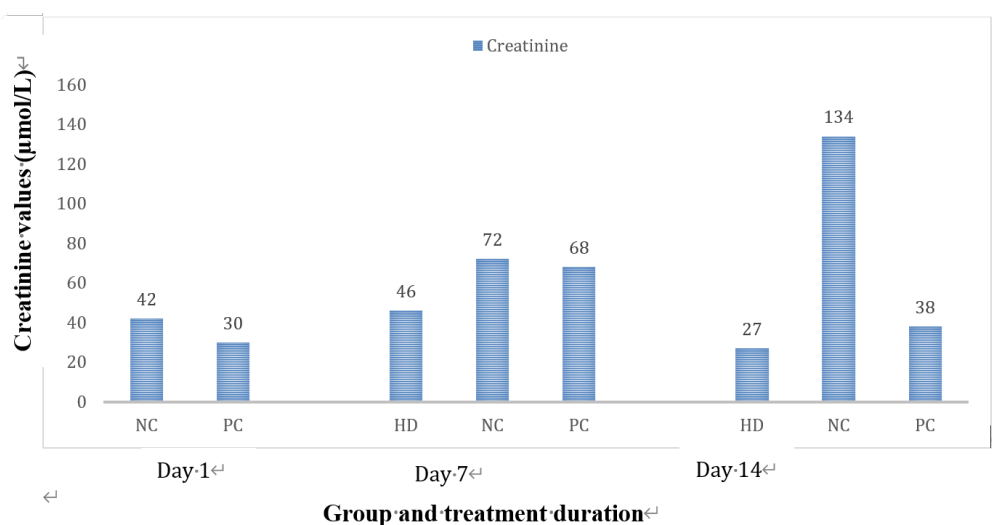
### 3.3. Effect of high-dose *Plectranthus ornatus* extract on creatinine levels

A noticeable increase in the creatinine level in both the negative and positive control groups on day 7, compared with day 1, with a sharp spike in the negative control group on day 14 of treatment. In contrast, creatinine levels in the positive control group remained relatively low on day 14, as did those in the high-dose treatment group.

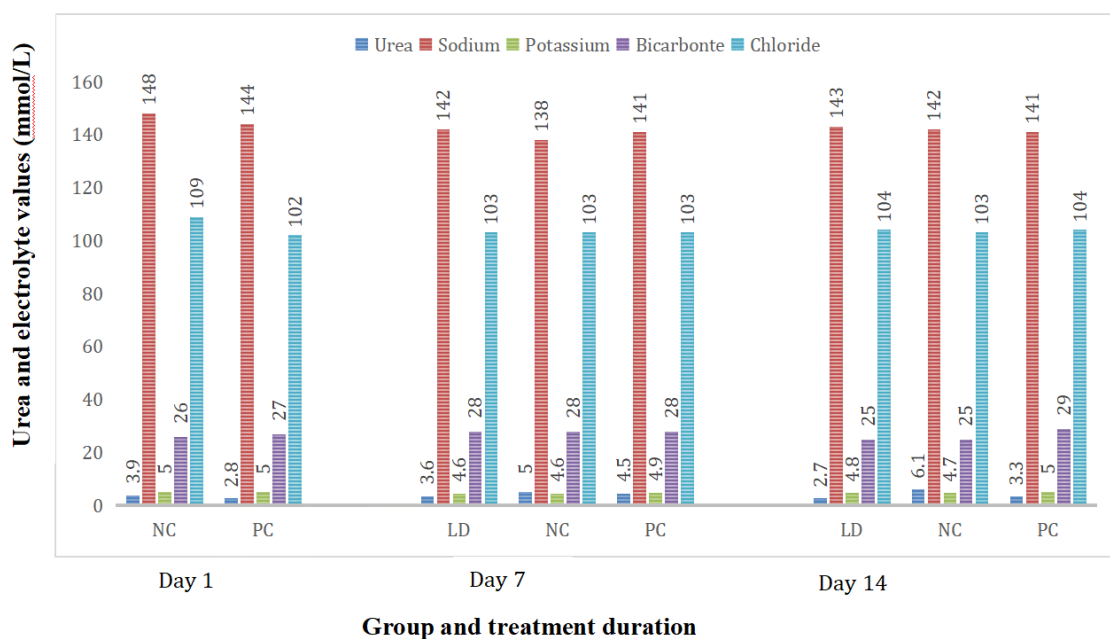
Additionally, the creatinine levels in rabbits treated with high-dose *P. ornatus* extract remained the lowest among all groups ([Figure 4](#)).

### 3.4. Effect of low-dose *Plectranthus ornatus* extract on kidney histology

Histological examination of the kidney section ([Figure 5A](#)) revealed the cortex containing several glomeruli and sections of the convoluted tubules, as well as a medullary zone characterized by linear medullary tubules. A mild inflammatory reaction was observed that could not be

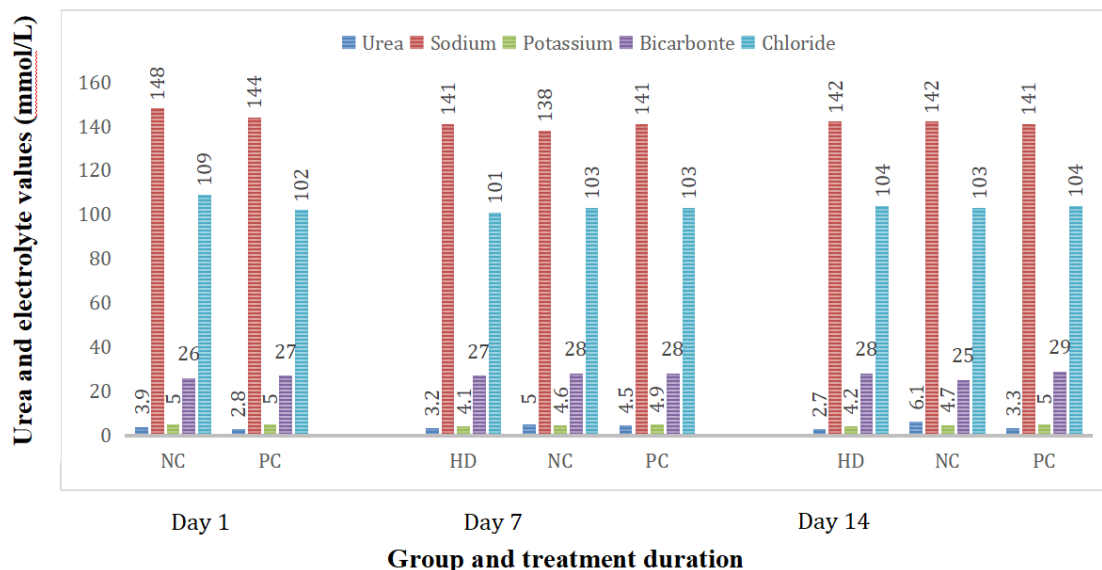


**Figure 1.** Blood pressure (mmHg) changes in the negative, positive, low-dose, and high-dose groups on days 1, 7, and 14 post-treatment  
Abbreviations: HD: High dose; LD: Low dose; NC: Negative control; PC: Positive control.



**Figure 2.** Urea and electrolytes (mmol/L) concentrations in negative, positive, and low-dose groups on day 1, day 7, and day 14 post-treatment  
Abbreviations: LD: Low dose; NC: Negative control; PC: Positive control.





**Figure 3.** Urea and electrolytes (mmol/L) concentration in negative, positive, and high-dose groups on day 1, day 7, and day 14 post-treatment  
Abbreviations: HD: High dose; NC: Negative control; PC: Positive control.

readily explained, as the rabbit had not received any treatment. In [Figure 5B](#), similar histologic features were noted, with distinct cortical and medullary regions and an accumulation of polymorphonuclear inflammatory cells in the medullary area. In [Figure 5C](#), inflammation appeared to be more pronounced, particularly around the cortex; however, by day 14 ([Figure 5D](#)), there was a marked reduction in the number of inflammatory cells.

### 3.5. Effect of high-dose *Plectranthus ornatus* extract on kidney histology

Histological examination of the kidney section revealed the cortex with several glomeruli and sections of the convoluted tubules, as well as a medullary zone indicated by linear medullary tubules. A mild inflammatory reaction was observed; however, this finding cannot be attributed to treatment, as the animal received no treatment ([Figure 6A](#)). In [Figure 6B](#), similar histologic features were evident, with distinct cortical and medullary regions and a concentration of polymorphonuclear inflammatory cells in the medullary area. Inflammatory cells are seen in the animals administered a high dose on days 7 and 14 post-treatment ([Figures 6C–6D](#)); however, the highest intensity was noted on day 14 in the high-dose group, suggesting that the extract may not be well tolerated at this concentration over a prolonged period.

### 3.6. Effect of low-dose *Plectranthus ornatus* extract on bladder histology

Histological examination of the bladder revealed an outer, slightly muscular layer with abundant connective tissue and an inner epithelial layer lined by transitional cells, showing generally normal histology ([Figure 7A](#)). In [Figure 7B](#), a similar normal histological appearance was observed, suggesting that dexamethasone-induced hypertension did not directly affect the bladder. In [Figure 7C](#), treatment with the extract appeared to cause mild swelling in both the epithelial and non-epithelial regions of the bladder, accompanied by slight inflammation in some tissue areas. In [Figure 7D](#), numerous cytoplasmic vacuolations were evident after 14 days of treatment, indicating tissue injury that may have resulted from prolonged exposure to the extract at the administered dosage.

### 3.7. Effect of high-dose *Plectranthus ornatus* extract on bladder histology

Histological examination of the bladder revealed an outer, slightly muscular layer with abundant connective tissue and an inner epithelial layer lined by transitional cells, showing generally normal histology ([Figure 8A](#)). [Figure 8B](#) similarly showed virtually normal histology, suggesting that dexamethasone-induced hypertension may not have directly affected the bladder. In the high-dose treatment group, by day 7, histological changes

indicate adverse effects on bladder structure (Figure 8C). By day 14 (Figure 8D), cytoplasmic vacuolations persisted, and the differences between these groups and the negative and positive controls were pronounced. The underlying connective tissue in both high-dose sections (Figures 8C–8D) appeared looser than in the control sections, suggesting possible tissue compromise associated with prolonged exposure to the high-dose extract.

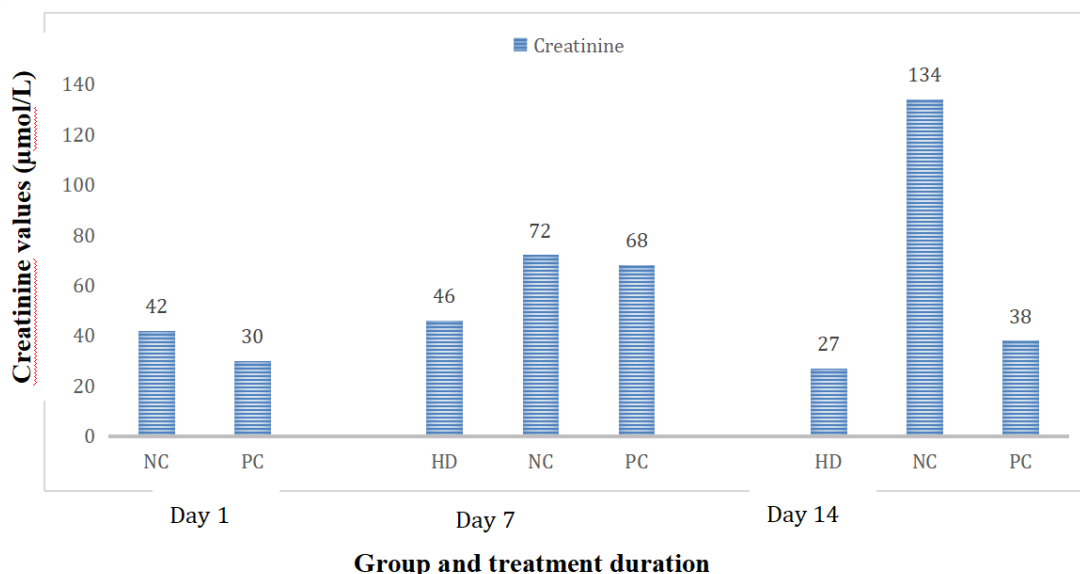
## 4. Discussion

The administration of *P. ornatus* to dexamethasone-induced hypertensive rabbits significantly altered blood pressure regulation. Dexamethasone, known for its hypertensive effects, caused elevated systolic and diastolic blood pressures in the positive control group on day 1, confirming the induction of hypertension, as documented in previous studies.<sup>17,24,25</sup> Conversely, the negative control group maintained lower blood pressure values, reflecting normotension. Administration of *P. ornatus* at a low dose (200 mg/kg) resulted in a modest reduction in both systolic and diastolic pressures by day 7, consistent with the antihypertensive effects reported for other medicinal plants.<sup>26,27,28,29</sup> A more pronounced hypotensive effect was observed with the high dose (1,000 mg/kg), indicating a dose-dependent response. The pronounced hypotensive effect supports the bradycardic effect of certain medicinal plants at higher dosages, as documented in another study.<sup>30</sup> By day 14, the low-dose group exhibited a more potent and

sustained reduction in blood pressure, even surpassing the effect of the high-dose group. This suggests that prolonged administration of *P. ornatus* at a lower dose may be more effective in managing hypertension, possibly due to a more favorable pharmacodynamic profile over time.

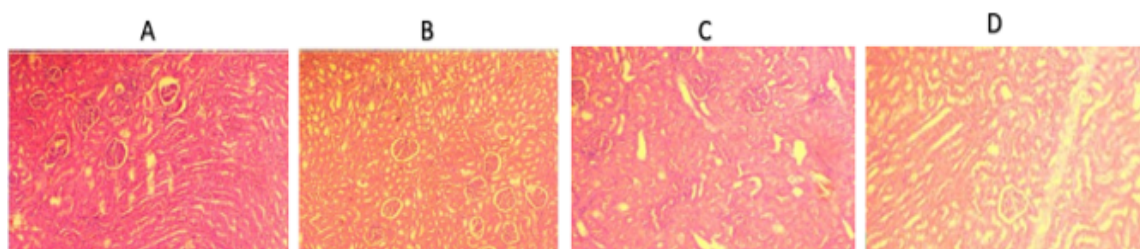
The biochemical analysis of renal function, including urea, electrolytes, and creatinine levels, provides crucial information about the nephroprotective or nephrotoxic effects of *P. ornatus*. The results indicated that urea and electrolyte levels in rabbits treated with *P. ornatus* remained within acceptable ranges compared with the control groups, suggesting that the extract did not significantly disrupt renal function at the tested doses. Aside from the experimental controls, the outcomes of this study are consistent with previous reports<sup>31,32,33</sup> on laboratory reference values for rabbits. However, creatinine levels in the positive control group increased over the study period, particularly on day 14, reflecting the renal impairment commonly associated with hypertension. Interestingly, rabbits treated with the extract at both low and high doses showed lower creatinine levels than the positive control, suggesting that *P. ornatus* has a protective effect against hypertension-induced renal damage.<sup>16</sup>

The low dose was particularly effective in maintaining lower creatinine levels, reinforcing the earlier observation that prolonged treatment with a lower dose may offer better renal protection.

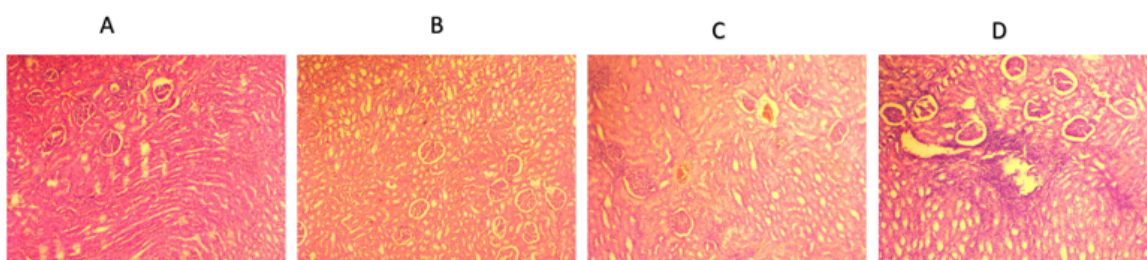


**Figure 4.** Creatinine (µmol/L) in rabbits treated with high-dose extract on day 1, day 7, and day 14 post-treatment  
Abbreviations: HD: High dose; NC: Negative control; PC: Positive control.

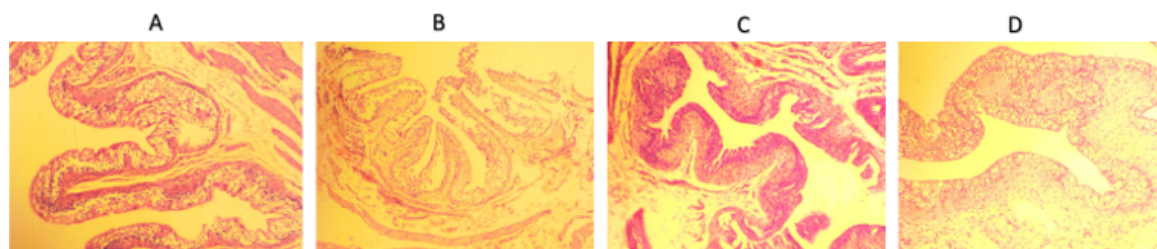




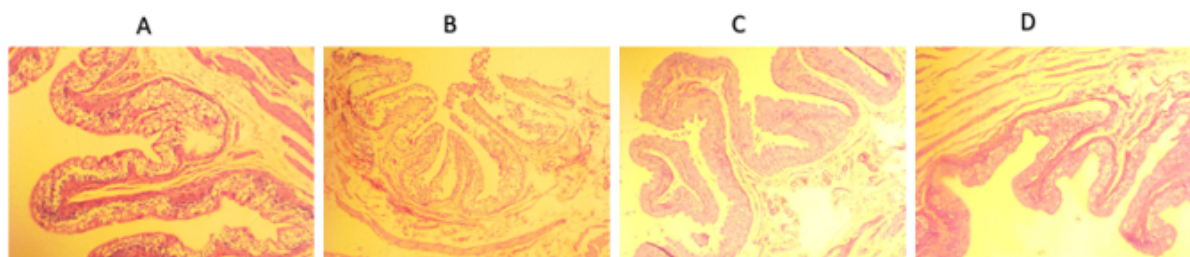
**Figure 5.** Kidney sections of rabbits treated with a low dose of *Plectranthus ornatus* extract. (A) Photomicrograph of the negative control kidney section on day 7 post-treatment. (B) Photomicrograph of the positive control kidney section on day 14 post-treatment. (C) Photomicrograph of the low-dose kidney section after 7 days of treatment. (D) Photomicrograph of the low-dose kidney section after 14 days of treatment. Hematoxylin & eosin; scale bar: 100  $\mu$ m; magnification:  $\times 100$ .



**Figure 6.** Kidney sections of rabbits treated with a high dose of *Plectranthus ornatus* extract. (A) Photomicrograph of the negative control kidney section on day 7 post-treatment. (B) Positive control kidney section on day 14 post-treatment. (C) High-dose kidney section after 7 days of treatment. (D) Photomicrograph of the high-dose kidney section after 14 days of treatment. Hematoxylin & eosin; scale bar: 100  $\mu$ m; magnification:  $\times 100$ .



**Figure 7.** Bladder sections of rabbits treated with a low dose of *Plectranthus ornatus* extract. (A) Photomicrograph of the negative control bladder section on day 7 post-treatment. (B) Photomicrograph of the positive control bladder section on day 14 post-treatment. (C) Photomicrograph of the low-dose bladder section after 7 days of treatment. (D) Photomicrograph of the low-dose bladder section after 14 days of treatment. Hematoxylin & eosin; scale bar: 100  $\mu$ m; magnification:  $\times 100$ .



**Figure 8.** Bladder sections of rabbits treated with a high dose of *Plectranthus ornatus* extract. (A) Photomicrograph of the negative control bladder section on day 7 post-treatment. (B) Photomicrograph of the positive control bladder section on day 14 post-treatment. (C) Photomicrograph of the high-dose bladder section after 7 days of treatment. (D) Photomicrograph of the high-dose bladder section after 14 days of treatment. Hematoxylin & eosin; scale bar: 100  $\mu$ m; magnification:  $\times 100$ .

Dexamethasone is a potent synthetic glucocorticoid that induces hypertension through mechanisms such as fluid retention, increased vascular resistance, and alterations in the renin-angiotensin-aldosterone system.<sup>25</sup> Histological analysis revealed significant pathological changes in the kidneys of dexamethasone-treated rabbits compared to the negative control group, consistent with previous reports on renal damage as a complication of hypertension.<sup>2,5,34,35</sup> The kidneys of the positive control group displayed mild inflammatory reactions, particularly within the medullary region, characterized by the infiltration of polymorphonuclear inflammatory cells.

These cells are markers of an immune response and are typically involved in the body's reaction to tissue damage or infection. The presence of these inflammatory cells suggests that dexamethasone-induced hypertension triggers a localized inflammatory response in the kidneys, which could be an early indicator of renal injury. The observed damage is consistent with Williams' report.<sup>5</sup> The presence of inflammation in the high dose post treatments underscores the effect of dexamethasone and the associated hypertensive state on renal morphology. The bladder tissue in the positive control group also showed notable changes compared to the negative control group. In the negative control rabbits, bladder histology appeared normal, with intact muscular and epithelial layers and no signs of inflammation or other pathological alterations. However, in the positive control group, despite the kidneys showing signs of inflammation, the bladder displayed a relatively normal histological appearance, with no significant alterations in the epithelial or muscular layers. This suggests that while dexamethasone-induced hypertension had a clear impact on renal histology, its effects on the bladder were less pronounced in the short term. The histological findings in the kidneys suggest that dexamethasone-induced hypertension initiates an inflammatory response that could potentially progress to more severe renal damage, such as fibrosis or glomerulosclerosis, if the hypertensive state persists. The inflammation observed could lead to compromised renal function over time, highlighting the kidneys' vulnerability to hypertensive injury. This outcome has also been similarly reported by Williams.<sup>5</sup>

On the other hand, the bladder's relative resistance to histological changes in the presence of dexamethasone-induced hypertension may indicate that it is less susceptible to early hypertensive damage than the kidneys. However, the absence of significant changes in bladder histology does not rule out the possibility of long-term damage if the hypertensive state is maintained.

Dexamethasone-induced hypertension has a pronounced impact on the renal histology of experimental

rabbits, as evidenced by the inflammatory changes observed in the kidneys. Although the bladder did not show significant histological alterations in this study, the findings suggest that sustained hypertension may eventually lead to pathological changes in the bladder. These results underscore the importance of managing hypertension to prevent long-term damage to both the kidneys and the bladder.

Histological analysis of the kidney and bladder revealed the impact of both dexamethasone-induced hypertension and *P. ornatus* treatment on renal morphology.

In the negative control group, the renal histology revealed normal architecture with well-defined glomeruli and tubules. However, the positive control group exhibited mild inflammatory reactions in the medullary region, possibly due to the dexamethasone-induced hypertensive state. The damage observed in the studied animals is consistent with a documented study by Williams<sup>5</sup>. In the low-dose treatment group, inflammation was more pronounced in the cortex by day 7, but marked reductions in inflammatory cells were observed by day 14. This suggests that *P. ornatus* possesses an anti-inflammatory effect over time, particularly at lower doses. The healing properties of this plant have been demonstrated by numerous studies.<sup>9-13</sup> In contrast, the high-dose group exhibited intense inflammation by day 14, suggesting that the extract at this concentration may not be well tolerated for extended periods, potentially leading to nephrotoxicity.

The bladder histology in the negative control group appeared normal, with no significant pathological changes. The positive control group also displayed normal histology, suggesting that dexamethasone-induced hypertension did not directly affect the bladder. However, treatment with *P. ornatus* at both low and high doses led to noticeable histological changes. The low-dose group exhibited swelling in both epithelial and non-epithelial regions of the bladder by day 7, with inflammation intensifying by day 14. The high-dose group showed even more pronounced vacuolations and loosening of connective tissues, indicating tissue injury likely due to prolonged exposure to the extract. These findings suggest that while *P. ornatus* may have therapeutic potential; its use should be carefully monitored to avoid renal and bladder toxicity, particularly at higher doses and with prolonged use.

## 5. Conclusion

*Plectranthus ornatus* extract demonstrates a high safety margin with an LD<sub>50</sub> exceeding 5,000 mg/kg. The extract exhibits antihypertensive effects, particularly at lower doses administered over prolonged periods, and provides some renal protection against dexamethasone-induced

hypertension. However, the potential for nephrotoxicity and bladder injury at higher doses or with extended use warrants caution. These findings suggest that *P. ornatus* may be a promising candidate for managing hypertension, but further studies are needed to fully understand its long-term safety and efficacy.

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## Conflict of interest

The authors declare they have no competing interests.

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## Ethics approval and consent to participate

The paper describes a study that involves experimental animals. Ethical clearance (approval: UJ/FPS/F17-00379) for the use of laboratory animals was obtained from the Ethical Committee, Department of Pharmacology, University of Jos.

## Consent for publication

Not applicable.

## Availability of data

Data used in the study can be obtained from the corresponding author on reasonable request.

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