

Evaluation Of Haematological Effect and Testosterone Levels in *Rattus Norvegicus* Administered *Pausinystalia Yohimbe*

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ABSTRACT

This study focused on the effects of *Pausinystalia yohimbe* ethanolic extract on the hematological parameters and testosterone levels in Wistar rats. Forty-two rats were grouped into six groups (A–F) of seven animals each (4 males and 3 females) and were administered *P. yohimbe* extract at doses of 25 mg/kg, 50 mg/kg, 75 mg/kg, and 100 mg/kg, with a positive control group receiving Sildenafil citrate at 5 mg/kg and a negative control group receiving distilled water for 14 days. The rats were sacrificed, and 5 ml of blood was collected for hematology tests. There was an increase in hematological parameters (PCV, WBC, hemoglobin, and lymphocytes) as the concentration of *P. yohimbe* extract increased, except for RBC and platelet levels which decreased. RBC levels decreased from (8.80 ± 0.12) at 25 mg/kg to (8.52 ± 0.02) at 100 mg/kg compared to the control (8.70 ± 0.06) . Platelet levels decreased from (764.00 ± 0.58) at 25 mg/kg to (5.70 ± 1.73) at 100 mg/kg compared to the control (532.00 ± 1.15) . There was a significant increase in testosterone levels with increasing concentrations of the extract: 25 mg/kg (8.52 ± 0.02) and 50 mg/kg (6.70 ± 0.06) , but a decrease at 100 mg/kg (5.40 ± 0.12) compared to the control (3.00 ± 0.12) . The study reveals that *P. yohimbe* ethanolic extracts have a significant effect on the hematological parameters and testosterone levels of Wistar rats.

Keywords: Stem bark, *Pausinystalia yohimbe*, hematological parameters, testosterone levels, Wistar rat.

1.0 INTRODUCTION

Yohimbe, known scientifically as *Pausinystalia yohimbe*, is an evergreen tree whose bark has been used for centuries in Africa to treat a range of conditions such as coughs, fevers, heart disease, and even leprosy. Traditionally, the bark extract has also been valued for its aphrodisiac properties and used as a hallucinogen and anesthetic. Today, in Western countries, yohimbe is commonly used to help with erectile dysfunction. (European Food Safety Authority, 2009). *Pausinystalia yohimbe* is a species of tree in the Rubiaceae family, native to tropical West Africa. The principal plant part used medicinally is the stem bark, which contains indole alkaloids including yohimbine as the main active compound. The alkaloid concentration increases as the branches ages (European Food Safety Authority, 2009). Yohimbe is a tree that stands out with its whorled branches at the top and can grow anywhere from 9 to 30 meters tall. Its trunk is straight and unbuttressed, reaching up to 50 centimeters in diameter (Raponda-Walker et al., 1961). In Africa, yohimbe is a popular medicinal herb, often harvested from the wild for local use and widely sold in local markets. It's been valued for centuries in western Africa as a male aphrodisiac and a mild hallucinogen. More recently, it has gained scientific recognition in the West for treating impotence and enhancing sexual stimulation. (Ojatula, 2023).

Yohimbe is a compound found in several biological sources, known for its powerful pharmacological effects. It belongs to a group of chemicals called monoterpene indole alkaloids. (Yang et al., 2021). Yohimbe, also known as quebrachine, aphrodine, corynine, and hydroaerogotocin, is part of a large class of medicinal compounds known as indole-based pharmacological medicines. Recent advances have expanded their use in modern therapeutics (Kumar, 2021; Qin et al., 2021). It has also been used as a stimulant and aphrodisiac to enhance sexual function.

Yohimbe, a prototypical α_2 -receptor antagonist, has been licensed in Germany since 1978 and in Canada since 1951 as a treatment for erectile dysfunction. (Wibowo et al., 2021). It has been used as a treatment for sexual problems for several decades. It is a reasonably safe medicine, with minimal reported side effects. (Ojatula et al., 2020). The hyperadrenergic properties are advantageous in treating several medical conditions, including erectile dysfunction, myocardial dysfunction, inflammatory disorders, and cancer. (Kawano et al., 2021; Wibowo et al., 2021 and Paciaroni et al., 2020). In the study by Osonuga et al. (2020), Effects of Aqueous Leaf Extract of *Telfairia occidentalis* on haematological parameters and Liver Enzymes in Male Wistar Rats,

found that the administration of the aqueous extract of *Telfairia occidentalis* resulted in a dose-dependent increase in various blood parameters. Specifically, the extract caused significant elevations in red blood cell count, white blood cell count, and packed cell volume. Similarly, Onyeabo *et al.* (2017) performed a haematological and biochemical research on *Justicia carnea* leaves extract in phenylhydrazine-induced anemia in wistar rats. They found that Packed Cell Volume (PCV), Red Blood Cell (RBC) count, and hemoglobin (Hb) concentrations significantly decreased ($p < 0.05$) 48 hours after phenylhydrazine induction. However, after 28 days of administering *Justicia carnea* extracts, PCV values, RBC count, and Hb levels significantly increased ($p < 0.05$). Also, the studies of Gofwan *et al.* (2021) reported the aqueous extract of *Parquetina nigrescens* root in Wistar rats resulted in significant increases in testosterone levels. However, the objective of this study is to evaluate the stem bark activity of *P. yohimbe* on blood parameters, including white blood cell (WBC) count, red blood cell (RBC) count, hemoglobin levels, PCV, lymphocytes, and platelets.

1.1 AIM AND OBJECTIVES OF THE RESEARCH

The aim of this study is to evaluate the hematological effects and testosterone levels of *Pausinystalia yohimbe* in *Rattus norvegicus* after administration.

The specific objectives are:

1. To examine the effects of *Pausinystalia yohimbe* on the hematological parameters of male Wistar albino rats through a full blood count analysis.
2. To determine the serum testosterone levels in male Wistar albino rats following the administration of *Pausinystalia yohimbe*, focusing on its potential aphrodisiac effects

2.0 MATERIALS AND METHODS

2.1 Study Area

The Stem bark of *Pausinystalia yohimbe* plants were collected from traditional healers in Kasuwar Magani, Amaru, Zaria City, Kaduna State, Nigeria. Zaria city is located in Zaria local government area of Kaduna State. It is located in (GL). The plants collected were then transported to the Department of Botany Ahmadu Bello University, Zaria for proper identification and authentication with voucher number ABU02876.

2.2 Plant preparation and Extraction

Using a clean laboratory mortar and pestle, the collected plant material was grounded into a fine powder and air-dried at a temperature of 25°C. An ethanolic extraction method was employed to obtain the crude extracts of *P. Yohimbe*. To ensure consistency in the crude extracts, the powdered sample was soaked in a mixture of distilled water and 80% ethanol. A total of 500 grams of the powder was weighed and immersed in 1000 ml of solvents for 72 hours, with occasional shaking. Initially, the mixture was filtered through gauze, and the filtrate was subsequently passed through a sterile Whatman filter (England). The resultant filtrate was then dried using a rotary evaporator at 38.5–40°C and further dried in an oven at 40°C. The dried extracts were weighed, documented, and stored in a refrigerator until needed. Prior to administration, all doses of Yohimbe extracts were diluted in distilled water.

2.3 Identification and Selection of Animal Models

Male adult wistar rats, weighing 30–35g and of 12 weeks of age, with female adult wistar rats weighing 26–30g were purchased from a standard Laboratory in Veterinary Physiology Department A.B.U, Zaria. The animals were placed in a conventional environment (inverted 12 h: 12 h light: dark cycle) at a temperature of $25 \pm 2^\circ\text{C}$, and they were fed a standard laboratory mice food until they were full. Before the experiment, the animals were given two weeks to get used to their new environment (acclimatization).

2.4 Experimental Design

Forty-two wistar rats were categorized into six groups (A–F) of seven animals each (4 males and 3 females). Each group was kept in a separate polypropylene cage with sawdust that was replaced every day. All groups were treated as Group A (Negative Control): with 0.5 ml of distilled water Group B (Positive Control): Sildenafil citrate 5mg/kg, Group C, Group D, Group E and Group F.

2.5 Administration of Oral Doses of *P. yohimbe* Ethanolic Extracts

The standard dosages of Yohimbe extract (yohimbine content) were diluted with distilled water to achieve the desired concentration for accurate dosing ranging from 25 mg to 100 mg per day, for fourteen days according to the procedure of Yakubu and Quadri (2012).

2.6 Haematological Analysis

After two weeks of administration, the Wistar rats were sacrificed following anesthesia with chloroform. A 5 ml blood sample was collected from each rat through heart puncture. From the total blood collected, 1 ml was transferred into a labeled container containing

ethylenediamine tetra acetic acid (EDTA) as an anticoagulant. This sample was used for hematological investigations, including red blood cell (RBC) count, white blood cell (WBC) count, hemoglobin (Hb) concentration, packed cell volume (PCV), and platelets. The hematological study was performed using a hematology auto-analyzer (Dacie and Lewis, 1994).

2.7 Determination of Testosterone Level

To determine the testosterone level, a Microplate Enzyme Immunoassay Kit, specifically designed to measure total testosterone concentration in human serum was used. Following the manufacturer's test protocol, quantification of the serum testosterone concentrations using the Accu-Blind ELISA Microwells (Product Code: 3725-300) from Monobind Inc., USA was done.

2.9 Data Analysis

The data obtained was statistically analyzed using one way analysis of variance (ANOVA) followed by post hoc test least significant difference (LSD) to determine the significance between effects resulting from exposure of the test and the control at significant level of $p < 0.05$ and was expressed as mean \pm standard deviation (SD) and statistical package for social science (SPSS) was used for the analysis.

3.0 RESULTS AND DISCUSSION

Humans have been using medicinal plants for ages in traditional medicine due to their therapeutic potential. Contemporary research on these plants has led to the discovery of new drug candidates that are effective against various diseases (Akhtar *et al.*, 2020). According to the World Health Organization WHO (2008), more than 80% of the global population depended on traditional medicine for their primary healthcare needs. The increasing reliance on traditional medicine highlights the growing recognition of herbal medicine as a viable alternative form of healthcare. The screening of medicinal plants for bioactive compounds has become essential, as these plants offer valuable sources of data for the development of antibiotics and other therapeutic prototypes (Pandey *et al.*, 2021). Table 1. Presents the Effect of *Pausinystalia Yohimbe* extract on hematological parameters of male Wistar Albino Rats (Full Blood Count). After 14 days of the administration, the hematological parameters shows an increase in Packed cell volume (PCV) level ($p \leq 0.05$) when compared to the control from (40.30 ± 0.12) to the highest (47.20 ± 0.23) at 75 mg/kg body weight with ethanolic extract. Similarly, Salami and Ewuola (2015) evaluated the methanolic extract of *Paullinia pinnata* and revealed that PCV values increased significantly at doses of 50, 100, and 400 mg/kg body weight, while a decrease was noted at 200 mg/kg. The study concluded that the extract has

erythropoietic properties, as evidenced by elevated PCV and Hb levels in treated rats, suggesting enhanced blood formation. Also, Ikese *et al.* (2020) reported the effects of *Telfairia occidentalis* leaf extract were also studied, particularly in rats with malaria-induced anemia. The extract led to a 22% increase in post-inoculation PCV over five days, contrasting with declines observed in control groups. The study highlighted the extract's potential to boost iron levels, crucial for hemoglobin formation and red blood cell production, thereby improving PCV in anemic conditions. Furthermore, for the white blood cells (WBC), there was a significant increase when administered with the methanolic extracts of *P. yohimbe* compared to the control group. The control group showed an increase at all dosage levels (4.31 ± 0.01) while the *P. yohimbe* extract at 100 mg/kg resulted in a significantly higher count of 9.23 ± 0.03 ($p < 0.05$). This aligns with the study of Ofem and Eno (2012) on the aqueous leaf extract of *Ocimum gratissimum* showed that while there were no significant changes in total WBC counts among different groups of rats, there were notable variations in differential counts. The high-dose group exhibited a significant increase in neutrophils and a decrease in lymphocytes compared to the low-dose group. This suggests that *O. gratissimum* may modulate immune responses by affecting specific types of white blood cells, particularly increasing neutrophils, which are crucial for fighting infections. Similarly Taiwo and Garuba (2009) examined the effects of *Viscum album* extracts from different host plants. The results indicated an increase in WBC counts in rats, suggesting that the mistletoe extract may stimulate leucocyte production, potentially serving as an immune booster. For the RBC, there was slight decrease in red blood cell (RBC) count than the control group. A decrease in the hemoglobin level at 25 mg/kg (12.41 ± 0.02) and 12.41 ± 0.02 and 50 mg/kg (12.96 ± 0.13) and 13.00 ± 0.17) doses of the extract, compared to the control (13.40 ± 0.17) was observed. However, there was a significant increase in haemoglobin levels at 75 mg/kg and 100 mg/kg doses of the extract when compared to the control. The findings of this study suggest that there was increase in haemoglobin level as concentration of *P. yohimbe* methanolic extract increases. The ethanolic leaf extract of *Gongronema latifolium* was also found to reduce RBC, Hb, and other hematological parameters. The reduction was linked to the presence of saponins in the extract, which may hinder the development of blood cells in the bone marrow (Akinnuga *et al.*, 2011). In contrast, *Moringa oleifera* extracts have shown positive effects on hematological parameters, significantly increasing Hb and RBC counts in treated rats. This suggests that while some plant extracts can decrease RBC counts, others may enhance blood production and overall hematological health (Otitoju *et al.*, 2014). Furthermore,

for the blood platelets level, there was a progressive increase in blood platelets level with decrease in administration of *P. yohimbe* methanolic extract when compared to the Positive control (Sildenafil Citrate). Research has demonstrated that various plant extracts can positively influence platelet counts in rat models, particularly in conditions such as thrombocytopenia. Apostol *et al.* (2018) investigated the effects of *Euphorbia hirta* on ethanol-induced thrombocytopenic in rats. The results indicated a significant increase in platelet counts among the rats treated with this extract. Additionally, there was a noted decrease in both bleeding and clotting times, suggesting that *Euphorbia hirta* may enhance hemostatic function in thrombocytopenic conditions. The aqueous leaf extract of *Ocimum gratissimum* was found to increase platelet counts significantly in a study involving male Wistar rats. The high-dose group (1000 mg/kg) exhibited elevated levels of red blood cells, packed cell volume, hemoglobin, and platelets compared to control groups. This suggests that the extract may contain compounds that stimulate platelet production or release (Ofem and Eno, 2012).

For the lymphocytes level, the administration *P.yohimbe* methanolic extract in the group of rats at 25mg/kg body resulted in increase in the lymphocytes level (5.50 ± 0.06) while the highest level of lymphocytes were recorded in the group of 100mg/kg administered with

P.yohimbe methanolic extract. There was a general increase in lymphocytes level with increase in the plant extracts dose. Several studies have demonstrated that plant extracts can lead to an increase in lymphocyte levels in rats. According to Oluyele *et al.* (2020) an ethanolic leaf extract of *Bidens pilosa* demonstrated a significant increase in lymphocyte counts in Swiss albino rats. The study indicated that the extract has lymphopoietic and possible immunomodulatory effects, enhancing the immune response in treated groups compared to untreated ones. The infected-untreated group showed a decline in lymphocyte count, highlighting the extract's potential in promoting lymphocyte production and overall immune function. Similarly, Otitoju *et al.* (2014) evaluated the aqueous leaf extract of *Moringa oleifera* and reported increases in lymphocyte counts among Wistar rats. This plant is known for its nutritional and therapeutic properties, and its extract has been suggested to stimulate hematopoiesis, thereby enhancing lymphocyte production and contributing to improved immune response. Izam and Aguiyi (2021) reported that the leaf extract of *Carissa edulis* was shown to increase lymphocyte levels in rats treated with carbon tetrachloride (CCl₄), which typically reduces lymphocyte counts due to its toxic effects. The extract's ability to activate immune effector cells contributed to the observed increase in lymphocyte levels, suggesting its protective role against immune suppression.

Table 1: Effect of *Pausinystalia Yohimbe* on Haematological/Blood parameters of male Wistar Albino Rats (Full Blood Count)

Treatment Groups	PCV (%)	White blood cell (103/ul)	Red blood cell (106/ul)	Haemoglobin (g/dl)	Platelets (103/ul)	Lymphocytes (103/ul)
Group A (Distil water)	40.10±0.17 ^c	3.23±0.10 ^g	5.70±0.12 ^c	12.21±0.05 ^f	886.00±0.58 ^a	3.20±0.12 ^d
Group B (SC)	40.30±0.12 ^c	4.31±0.01 ^f	8.70±0.06 ^{ab}	13.40±0.17 ^{cd}	532.00±1.15 ^h	5.50±0.06 ^{ab}
Group C (25mg/kg) Ethanolic	40.32±0.12 ^c	4.30±0.12 ^f	8.80±0.12 ^{ab}	12.50±0.12 ^{ef}	764.00±0.58 ^b	5.50±0.12 ^{ab}
Group D (50mg/kg) Ethanolic	44.30±0.06 ^b	5.63±0.04 ^e	8.72±0.01 ^{ab}	13.00±0.17 ^{de}	633.00±1.15 ^d	5.10±0.06 ^c
Group E (75mg/kg) Ethanolic	47.20±0.23 ^a	6.56±0.03 ^c	8.45±0.03 ^b	14.20±0.06 ^a	598.00±1.15 ^f	5.24±0.02 ^{bc}
Group F (100mg/kg) Ethanolic	46.67±0.51 ^a	9.23±0.03 ^a	8.52±0.02 ^{ab}	13.96±0.13 ^{ab}	570.00±1.73 ^g	5.65±0.02 ^a
Total	43.46±0.53	5.73±0.32	8.41±0.17	13.24±0.14	658.90±19.36	5.21±0.13
p Value	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*

* - Means along columns with different superscript(s) are significantly different at $p \leq 0.05$ according to DMRT

3.2 Testosterone

Table 2. presents the serum testosterone level of wistar rats administered with *P. yohimbe* ethanolic extract. There was increase in the level testosterone in wistar rats administered with *P. yohimbe* ethanolic extract than the

sildenafil citrate control group. The serum testosterone level was highest with *P. yohimbe* ethanolic extract at dose 50mg/kg (6.70 ± 0.06) as compared to the control group of sildenafil citrate (3.00 ± 0.12). The effect exhibited was of better chances than that of Sildenafil Citrate. This aligns with the work of Boublata *et al.* (2021) on the effects of ethanolic extract of *Cleome arabica* on sexual behavior and testosterone levels in male Wistar rats, the results showed that the extract significantly increased testosterone levels in the treated groups compared to the control group. Another study showed that an aqueous extract of *Imperata cylindrica* root increased testosterone levels in rats that had compromised testosterone due to Alloxan treatment. The extract caused dose-dependent increases in testosterone, which were statistically significant compared to the control group after 28 days of treatment. (Nwokike *et al.*, 2020).

Table 2: Assessment of the Serum Testosterone Level of Male Wistar Rats Due To Aphrodisiac

Treatment Groups	Testosterone
Group A (Distil water)	2.30 ± 0.12^f
Group B (SC)	3.00 ± 0.12^f
Group C (25mg/kg) Ethanolic	6.60 ± 0.12^a
Group D (50mg/kg) Ethanolic	6.70 ± 0.06^a
Group E (75mg/kg) Ethanolic	5.90 ± 0.12^b
Group F (100mg/kg) Ethanolic	5.40 ± 0.12^c
Total	4.52 ± 0.28
p Value	<0.001*

* - Means along columns with different superscript(s) are significantly different at $p \leq 0.001$ according to DMRT

4.0 CONCLUSIONS

This study reveals that *P. Yohimbe* ethanolic extracts have significant effect on the hematological parameters with increase in PCV (47.20 ± 0.23) at 75mg/kg, WBC counts (9.23 ± 0.03) at 25mg/kg, RBC (8.80 ± 0.12) at 25mg/kg, hemoglobin (14.20 ± 0.06) at 75mg/kg, Platelets (764.0 ± 0.58) at 25mg/kg, and lymphocyte levels (5.65 ± 0.02) at 100mg/kg in a dose-dependent manner compared to control groups and the serum testosterone levels (6.70 ± 0.06) at 50mg/kg of the wistar rats

5.0 RECOMMENDATIONS

1. Further study, should conduct additional studies to understand the biochemical and molecular mechanisms through which *P. Yohimbe* extracts affect hematological parameters and testosterone levels.
2. Further studies should evaluate the toxicological effects of *P. Yohimbe* extracts for assessing the safety and efficacy of the extracts over prolonged use.

3. Investigate whether there are sex differences in the response to *P. Yohimbe* extracts. This can provide insights into whether the effects observed in male Wistar rats are consistent in females, which is crucial for potential clinical applications.

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