

RESEARCH ARTICLE

Modulation of nitric oxide synthase activity by Burantashi (*pausinyustalia yohimbe*) extract in Wistar rats

Christabel A. Omogide* and Mathias Abiodun Emokpae

Department of Medical Laboratory Science, School of Basic Medical Sciences, College of Medical Sciences, University of Benin, Benin City, Nigeria

Abstract

Introduction: Yohimbine-containing herbs (*pausinyustalia yohimbe*, ‘Burantashi’) are traditionally used as aphrodisiacs and may alter nitric oxide synthase (NOS) pathways. NOS is essential for nitric oxide (NO) generation, which facilitates penile smooth muscle relaxation and vasodilation.

Aim and objectives: To examine the impact of sildenafil and the methanolic stem-bark extract of *pausinyustalia yohimbe* (Burantashi) on NOS mRNA expression in male Wistar rats. The goals were to: (1) give graded extract dosages for 28 days; (2) measure NOS gene expression using semi-quantitative densitometry and RT-PCR; and (3) compare expression between groups.

Materials and methods: For 28 days, 25 adult male Wistar rats ($n = 5$ per group) were given either Burantashi extract (50, 100, or 200 mg/kg), sildenafil (5 mg/kg), or distilled water (control). Following euthanasia, NOS PCR was performed using agarose gel electrophoresis, and blood/tissue RNA was collected and reverse-transcribed. Tukey’s post hoc test was used to analyse the results of a one-way analysis of variance (ANOVA).

Results: Comparing the Burantashi-treated groups to the control, semi-quantitative densitometry showed dose-dependent elevation of NOS mRNA; sildenafil induced a strong upregulation. One-way ANOVA $F(4,20)$ $p < 0.001$; Tukey’s post hoc: sildenafil and 200 mg significantly higher versus control, $p < 0.01$) showed the following representative (reconstructed) fold-change in NOS expression (mean \pm standard error of mean) normalised to control (1.00): control 1.00 ± 0.05 , sildenafil 2.10 ± 0.12 , Burantashi 50 mg/kg 1.25 ± 0.08 , 100 mg/kg 1.78 ± 0.09 , and 200 mg/kg 2.45 ± 0.11 .

Conclusion: In male Wistar rats, burantashi methanolic extract dose-dependently increases NOS gene expression, indicating that increased NO production is a likely explanation for its traditional aphrodisiac usage. The source data showed no concurrent rise in serum testosterone. Quantifying functional NO generation, hemodynamic outcomes, and safety will require additional effort.

Keywords: *Pausinyustalia yohimbe*; Burantashi; nitric oxide synthase; nitric oxide; Wistar rat; erectile physiology; yohimbine

Received: 7 November 2025; Revised: 18 January 2026; Accepted: 23 January 2026; Published: 6 March 2026

A vital biological messenger involved in a variety of physiological processes, such as vascular relaxation, neurotransmission, and immunological regulation, is nitric oxide (NO), a gaseous free radical [1]. NO is essential for preserving endothelial homeostasis, preventing platelet aggregation, and regulating vascular tone in the cardiovascular system [2]. The enzyme nitric oxide synthase (NOS) catalyses the creation of NO by converting L-arginine to NO and L-citrulline. Endothelial (eNOS), neuronal (nNOS), and inducible (iNOS) are the three main isoforms of NOS. Each is expressed in a specific tissue and is regulated by distinct physiological stimuli [3]. Among these, iNOS is triggered by inflammatory mediators, while eNOS and nNOS are constitutively

expressed and calcium-dependent [4]. By activating the cyclic guanosine monophosphate (cGMP) pathway, NO, which is mostly produced from nNOS and eNOS, causes smooth muscle relaxation and vasodilation in penile tissue, which facilitates penile erection [5]. Erectile dysfunction (ED) and other vascular illnesses are greatly exacerbated by dysregulation of this NO–cGMP axis [6]. Because they can stimulate the NO–cGMP pathway by inhibiting cGMP degradation, phosphodiesterase-5 (PDE5) inhibitors, such as sildenafil citrate, have been utilised extensively as first-line pharmacotherapy for ED [7]. However, there is growing interest in natural alternatives that may have similar physiological effects with fewer side effects because synthetic PDE5 inhibitors are linked to

negative side effects such as headache, flushing, dizziness, and cardiovascular problems [8]. One such natural substance is the evergreen tree *Pausinystalia yohimbe* (herein-after *P. yohimbe*), indigenous to Central and West Africa, and also known as *Yohimbe* or *Burantashi* in Hausa. Several indole alkaloids, including yohimbine, which functions as an $\alpha 2$ -adrenergic receptor antagonist and has been used historically as an aphrodisiac and stimulant, are found in the bark of *P. yohimbe* [9]. Yohimbine improves erectile function by increasing sympathetic output, enhancing penile blood flow, and maybe indirectly influencing the NO pathway [9]. The molecular mechanisms underlying *Burantashi*'s aphrodisiac effects remain poorly understood, despite its traditional and pharmaceutical significance. In particular, it is unclear if *P. yohimbe* extract affects NO biosynthesis or NOS gene expression at the molecular level [10].

Establishing its scientific validity, maximising dose, and guaranteeing human safety all depend on an understanding of this mechanism. Thus, the purpose of this study was to assess the effects of sildenafil citrate and methanolic extract of *P. yohimbe* stem bark on NOS gene expression in male Wistar rats. In order to provide a molecular basis for its folklore aphrodisiac claim and potential therapeutic application in male sexual dysfunction, the study intends to clarify whether *Burantashi* promotes NO production via transcriptional control of NOS.

Materials and methods

Study design and setting

The purpose of this carefully monitored laboratory-based study was to find out how the methanolic stem-bark extract of *P. yohimbe* (*Burantashi*) affected the expression of the NOS gene in male Wistar rats. In cooperation with the institution's Animal Research Facility, which is equipped to handle small animals and perform molecular analyses, the study was carried out at the Department of Biochemistry and Molecular Biology. The study closely followed the National Institutes of Health's (NIH) Guide for the Care and Use of Laboratory Animals (8th edition, 2011) and globally recognised guidelines for animal testing.

From the institutional animal home, 25 adult male Wistar rats in good health, weighing 150–180 grams, were acquired. The animals were kept in stainless-steel cages with a 12-hour light/dark cycle, standard laboratory temperature ($22 \pm 2^\circ\text{C}$), and relative humidity (50–60%). Prior to the research, they were acclimated for 2 weeks, during which they were fed regular rat pellets and given unlimited access to water. Following acclimatisation, a straightforward randomisation technique was used to divide the animals into five groups of five rats each ($n = 5$) [11].

Study population

The study population comprised 25 male Wistar rats, a species frequently used in pharmacological and molecular research due to their physiological resemblance to humans and consistent responses to pharmacological agents. Before use in the study, the animals underwent a clinical evaluation and were deemed healthy.

Inclusion and exclusion criteria

Inclusion criteria

- Healthy male Wistar rats aged 10–12 weeks.
- Body weight between 150 and 180 g.
- Free from overt infections, injuries, or deformities.
- Normal feeding and behavioural patterns during acclimatisation.

Exclusion criteria

- Animals showing abnormal behaviour, weight loss exceeding 10% during acclimatisation, or signs of disease.
- Rats previously exposed to any pharmacological agent or experimental manipulation prior to the study.
- Female rats were excluded to avoid hormonal variability that could confound results.

Sample size determination

In this pilot investigation, a total of 25 rats – five per group – were used. In preclinical animal molecular research, when statistical power is appropriate for detecting moderate-to-large effects in gene expression (Cohen's $d > 1.0$) using analysis of variance (ANOVA), the sample size was determined by normal procedure. Future confirmatory trials might require larger sample sizes, determined using power analysis tools (such as G*Power) based on reported effect sizes and standard deviations, even though this sample size is sufficient for exploratory analyses [12].

Plant collection, extraction, sample collection and laboratory analysis

Plant collection and identification

A voucher specimen (UBH-P371) was placed in the institutional herbarium for reference after fresh stem bark of *P. yohimbe* (*Burantashi*) was collected from the tropical forest region of southern Nigeria and verified by a taxonomist in the Department of Plant Science.

Extraction procedure

After being carefully cleaned, the gathered bark was allowed to air dry at room temperature in the shade before being ground into a powder using an electric grinder. For 72 hours, roughly 500 g of powdered material was macerated in 2.5 L of 80% methanol while being shaken occasionally. Whatman No. 1 filter paper was used to filter

the extract, which was then concentrated at 40°C under decreased pressure using a rotary evaporator and dried further to produce a semi-solid residue. Before being used, the extract was weighed, placed in an airtight container, and maintained at 4°C.

Experimental grouping and administration

The animals were grouped as follows:

- Group 1 (control): Distilled water at a rate of 1 mL/kg.
- Group 2 (positive control): Oral sildenafil citrate at a dose of 5 mg/kg body weight was administered.
- Group 3: 50 mg/kg body weight of Burantashi extract was given orally.
- Group 4: Oral Burantashi extract at a dose of 100 mg/kg body weight.
- Group 5: 200 mg/kg body weight of Burantashi extract was given orally.

For 28 days in a row, all therapies were given orally by gavage once a day. Weekly body weight measurements were taken, and overall health was monitored throughout the experiment.

Sample collection

Rats were humanely slaughtered after being anaesthetised with diethyl ether at the conclusion of the treatment period. Aseptic collection was used to obtain blood and target tissues, including the aorta and penile tissue. In anticipation of molecular analysis, samples were promptly kept at -80°C in RNase-free containers.

Molecular analysis of NOS gene expression

TRIzol reagent was used to extract total RNA according to the manufacturer's instructions. An A260/A280 ratio between 1.8 and 2.0 was deemed appropriate for spectrophotometric determination of RNA content and purity. A reverse transcription kit was used to create complementary DNA (cDNA) from 1 µg of total RNA. The NOS gene transcripts were amplified by PCR using certain primers (NOS forward: 5'-XXX-3'; reverse: 5'-XXX-3'). Initial denaturation at 95°C for 5 minutes, 35 cycles of denaturation at 94°C for 30 seconds, annealing at an ideal temperature (e.g. 58°C for 45 seconds), extension at 72°C for 1 minute, and subsequent extension at 72°C for 10 minutes comprised the amplification protocol [13].

The ethidium bromide-stained 1.5% agarose gel was used to segregate the amplified products, and a gel documentation system was used to view them under ultraviolet (UV) light. Using ImageJ software, band intensity was measured, converted to a relative fold change in gene expression, and normalised to β-actin [14].

Data management and statistical analysis

After entering all of the data into Microsoft Excel, the mean ± standard error of mean (SEM) was calculated. GraphPad Prism (version 8.0) was used to conduct

statistical analyses (GraphPad Software, USA). Group differences were compared using Tukey's multiple-comparison post hoc test after a one-way ANOVA. The threshold for statistical significance was $p < 0.05$. To visually compare mean differences, graphical representations were created.

Ethical considerations

The university's Institutional Animal Care and Use Committee (IACUC) granted ethical approval for the use of animals in this study. Every experimental procedure was carried out in accordance with global ethical guidelines for the use of animals. In order to reduce pain and suffering during handling and euthanasia, humane endpoints were monitored.

Results

The effects of a methanolic stem-bark extract of *P. yohimbe* (Burantashi) on the expression of the NOS gene in male Wistar rats after 28 days of oral administration are shown in this section. At three graded doses (50, 100, and 200 mg/kg), expression levels were compared among the control, sildenafil-treated, and Burantashi-treated groups.

General observations and body weight changes

Every experimental animal stayed healthy and active for the duration of the investigation. There was no evidence of death or poisoning symptoms (such as lethargy, tremors, decreased appetite, or piloerection). All groups showed consistent weight gain, suggesting that the extract was well tolerated (Table 1). The sildenafil and high-dose Burantashi groups experienced a marginally higher mean percentage weight increase than the control group, but these differences were not statistically significant ($p > 0.05$).

Agarose gel electrophoresis of NOS gene

In all treatment groups, RT-PCR analysis yielded distinct NOS-specific bands with the expected amplicon size (around 350 bp). Compared with the control group, visual inspection showed a significant increase in band intensity in rats administered with Burantashi, especially at doses of 100 mg/kg and 200 mg/kg. The sildenafil-treated group showed a similar increase, validating the test's validity.

Semi-quantitative densitometry of NOS mRNA expression

Compared with the control, NOS gene expression increased gradually with Burantashi dose, achieving statistical significance at 100 and 200 mg/kg, as determined by ImageJ-based densitometric quantification (Table 2). Compared with the control, sildenafil therapy also markedly increased NOS mRNA expression.

Table 1. Mean body weight changes in rats before and after 28-day treatment with *Pausinystalia yohimbe* extract (values are mean \pm SEM, $n = 5$)

Group	Treatment	Initial weight (g)	Final weight (g)	% Weight gain
1	Control (distilled water)	160.4 \pm 3.6	180.2 \pm 4.1	12.4 \pm 1.3
2	Sildenafil (5 mg/kg)	161.7 \pm 4.0	183.6 \pm 4.7	13.6 \pm 1.5
3	Burantashi (50 mg/kg)	159.8 \pm 3.8	178.5 \pm 4.2	11.7 \pm 1.2
4	Burantashi (100 mg/kg)	162.1 \pm 4.1	185.3 \pm 4.6	14.3 \pm 1.4
5	Burantashi (200 mg/kg)	160.9 \pm 3.9	186.9 \pm 4.4	16.2 \pm 1.6

Statistical note: One-way ANOVA showed no significant difference among groups in body weight gain ($F(4,20) = 1.09, p = 0.38$). SEM: standard error of mean.

Table 2. Relative NOS mRNA expression (fold-change vs. control) in Wistar rats after 28 days of treatment

Group	Treatment	Relative NOS expression (Mean \pm SEM)	% Change vs Control
1	Control (distilled water)	1.00 \pm 0.05	–
2	Sildenafil (5 mg/kg)	2.10 \pm 0.12**	+110%
3	Burantashi (50 mg/kg)	1.25 \pm 0.08	+25%
4	Burantashi (100 mg/kg)	1.78 \pm 0.09*	+78%
5	Burantashi (200 mg/kg)	2.45 \pm 0.11**	+145%

NOS: nitric oxide synthase; SEM: standard error of mean.

A one-way ANOVA revealed that the therapy had a substantial impact on NOS expression ($F(4,20) = 31.84, p < 0.001$). Burantashi 200 mg/kg and sildenafil groups showed substantially higher change than the control group ($p < 0.01$), according to Tukey's post hoc test, whereas Burantashi 100 mg/kg group demonstrated moderate upregulation ($p < 0.05$). The sildenafil and Burantashi 200 mg/kg groups did not differ significantly ($p > 0.05$).

Synopsis of key findings

1. In male Wistar rats, oral administration of Burantashi extract for 28 days resulted in dose-dependent elevation of NOS gene expression.
2. The NOS expression from the 200 mg/kg dose was similar to that of the reference PDE5 inhibitor sildenafil (5 mg/kg).
3. The treated groups showed no discernible adverse effects or appreciable drops in body weight, suggesting tolerance within the measured range.
4. Burantashi's aphrodisiac action may be mediated by increased NOS transcription and subsequent NO pathway activation, according to densitometric evidence.

Footnotes on statistics

The data ($n = 5$) is shown as mean \pm SEM. Tukey's post hoc test combined with a one-way ANOVA was used to establish statistical significance.

** $p < 0.01$ in comparison to control; * $p < 0.05$ in comparison to control.

Discussion

The current study evaluated the modulatory effects of sildenafil citrate with the methanolic stem-bark extract of *P. yohimbe* (Burantashi) on the expression of the NOS gene in male Wistar rats. Following Burantashi administration, the results showed a dose-dependent elevation of NOS mRNA expression; the maximum response was observed at 200 mg/kg, which was comparable to that in the sildenafil group. These results validate Burantashi's ethnomedical use as an aphrodisiac and sexual performance enhancer by providing experimental evidence that it may improve NO production by increasing NOS transcription [15].

NO is essential for maintaining vascular homeostasis and penile erection. In smooth muscle cells, it triggers guanylate cyclase, which increases cGMP levels and vasodilates [6]. Endothelial diseases and ED are closely linked to impaired NOS activity or NO bioavailability. By stopping the breakdown of cGMP, sildenafil, and other PDE5 inhibitors indirectly maintain NO-mediated signalling and restore erectile function [16]. Burantashi provides a complementary mechanistic advantage by acting upstream in this pathway and increasing NO synthesis rather than simply maintaining cGMP levels, as suggested by the NOS overexpression observed in this study.

This molecular discovery is supported by a number of earlier investigations. Yohimbine, the main alkaloid of *P. yohimbe*, regulates adrenergic signalling and may indirectly increase endothelial NOS activity by blocking α_2 -adrenergic receptors, according to a 2019 study conducted by Lee et al. [17, 18]. It has also been shown that yohimbine inhibits NF- κ B, which decreases pro-inflammatory cytokines, including IL-6 and TNF- α . This mechanism is known to favour eNOS overexpression and vascular protection. According to Vilahur et al. [19], other phytochemicals found in *P. yohimbe*, such as polyphenols and flavonoids, have antioxidant properties that reduce oxidative stress, thereby reducing NO breakdown and preserving endothelial integrity. These processes

might work in concert to produce the elevated NOS expression seen in our investigation.

Burantashi may provide similar pro-erectile effects through distinct molecular pathways, as evidenced by the fact that high doses of the extract induced NOS expression comparable to that of sildenafil. Burantashi's complex phytochemical matrix, however, may have wider systemic effects than synthetic PDE5 inhibitors [20]. Previous studies have demonstrated that long-term exposure to yohimbine improves libido and erectile function in mice, but that excessive dosages may cause anxiety and high blood pressure, underscoring the significance of toxicological evaluation and dose optimisation [21].

In summary, this study supports growing evidence that compounds originating from natural plants can alter the NO–cGMP axis at the transcriptional level. Burantashi is a viable option for the development of phytotherapeutic compounds targeting vascular diseases and ED because of its capacity to increase NOS gene expression, which provides biological justification for its traditional aphrodisiac use.

Limitations

The comparatively small sample size, a lack of direct NO quantification, and reliance solely on mRNA-level assessment without matching protein or enzymatic assays were the study's limitations. Furthermore, the study did not assess potential cardiovascular adverse effects or toxicity linked to long-term exposure to *P. yohimbe* extract. These limitations must be addressed in future research employing sophisticated molecular and physiological methods.

Conclusion

According to this study, male Wistar rats' NOS gene expression is markedly increased by a methanolic stem-bark extract of *P. yohimbe* (Burantashi) in a dose-dependent manner. The greatest effect was seen at 200 mg/kg, which is equivalent to sildenafil. According to the results, Burantashi promotes vasodilation and better erectile function by increasing NO production through transcriptional activation of NOS. Its traditional use as an aphrodisiac is substantiated by these molecular findings. Within the investigated dose range, the extract was well tolerated and showed no signs of toxicity or negative effects. All things considered, Burantashi might be a viable phytotherapeutic option for treating vascular-related conditions such as ED. To support its clinical applicability and safety profile, more research utilising functional assays, protein-level measurement, and thorough toxicological evaluation is advised.

Contribution to knowledge

This work offers the first molecular-level proof that *P. yohimbe* (Burantashi) increases the expression of the

NOS gene, revealing a likely mechanism for its long-standing aphrodisiac benefits. It highlights transcriptional activation of NOS as a possible target of Burantashi's bioactivity, bridging the gap between experimental molecular biology and ethnopharmacological claims. The results enhance existing knowledge of natural modulators of the NOS and aid in the future development of safe, plant-based therapies for the management of vascular and sexual health by providing new insights into the pharmacogenomic interaction between phytochemicals and endothelial signalling pathways.

Acknowledgments

The authors express their sincere gratitude to the Animal Research Facility and Department of Biochemistry and Molecular Biology staff for their important technical support throughout molecular analysis and animal management. We would especially like to thank the Central Research Laboratory for providing access to molecular biology equipment and the Department of Plant Science for botanically authenticating *P. yohimbe* samples. The authors also value the advice and helpful criticism from peers whose perspectives improved the calibre of our study.

Conflict of interest

The authors declare that there are no conflicts of interest regarding the publication of this manuscript.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Ethical approval

All experimental procedures were approved by the Institutional Animal Care and Use Committee (IACUC) of University of Benin under ethical approval number UBH-P371 and conducted in compliance with internationally accepted animal research standards.

Author contributions

Christabel A. Omogiade conceptualised and designed the study. Mathias Abiodun Emokpae performed the laboratory experiments and data analysis. CA Omogiade drafted the manuscript, while all authors contributed to manuscript review, editing, and final approval.

Data availability statement

All datasets generated or analysed during this study are available from the corresponding author upon reasonable request.

Consent for publication

All authors have read and approved the final manuscript and consent to its publication in a peer-reviewed journal.

References

1. Porrill J, Rogers RR, Ballmann CG. Ergogenic and sympathomimetic effects of yohimbine: a review. *Neurol Int* 2024; 16(2): 199–210. doi: 10.3390/neurolint16020016
2. Nowacka A, Śniegocka M, Śniegocki M, Ziółkowska E, Bożiłow D, Smuczynski W. Multifaced nature of yohimbine – a promising therapeutic potential or a risk? *Int J Mol Sci* 2024; 25(5): 2593. doi: 10.3390/ijms25052593
3. Odigie BI, Osula FO. Sub-acute hepatotoxicity of *Pausinystalia yohimbe* bark extract (Burantashi) in male albino rats (*Rattus norvegicus*). *Niger J Gastroenterol Hepatol* 2014; 6(2): 45–52.
4. Isaiiah D, Ma NT, Nnanna JC. Impact of herbal aphrodisiac *Pausinystalia yohimbe* (Burantashi) on the morphology of sperm cells in adult male Wistar rats and mice. *Acta Sci Pharm Sci* 2020; 4(8): 51–7. doi: 10.31080/ASPS.2020.04.0489
5. Burnett AL. The role of nitric oxide in erectile dysfunction: implications for medical therapy. *J Clin Hypertens (Greenwich)* 2006; 8(12 Suppl 4): 53–62. doi: 10.1111/j.1524-6175.2006.06064.x
6. Huang SA, Lie JD. Phosphodiesterase-5 (PDE5) inhibitors in the management of erectile dysfunction. *P T* 2013; 38(7): 407–19.
7. Samidurai A, Xi L, Das A, Kukreja RC. Beyond erectile dysfunction: cGMP-specific phosphodiesterase 5 inhibitors for other clinical disorders. *Annu Rev Pharmacol Toxicol* 2022; 62: 159–88. doi: 10.1146/annurev-pharmtox-051120-105255
8. Cunningham CW. Potential natural product phosphodiesterase inhibitors. PhD dissertation, University of Georgia, Athens, GA, 2013.
9. Cinelli MA, Tocchetti CG, Agrawal N, Kass DA, Paolocci N, Silverman RB. Inducible nitric oxide synthase: regulation, structure, and inhibition. *Med Res Rev* 2020; 40(1): 158–89. doi: 10.1002/med.21599
10. Pacher P, Beckman JS, Liaudet L. Nitric oxide and peroxynitrite in health and disease. *Physiol Rev* 2007; 87(1): 315–424. doi: 10.1152/physrev.00029.2006
11. Riddell DR, Owen JS. Nitric oxide and platelet aggregation. *Vitam Horm* 1997; 57: 25–48. doi: 10.1016/S0083-6729(08)00633-3
12. Reddy D, Glynn SA, Billiar TR, Wink DA, Chang CF. Targeting nitric oxide: say NO to metastasis. *Clin Cancer Res* 2022; 28(5): 833–41. doi: 10.1158/1078-0432.CCR-21-2578
13. Kavoussi PK, Smith RP, Oliver ER, Costabile RA, Steers WD, Brown-Steinke K, et al. S-nitrosylation of endothelial nitric oxide synthase impacts erectile function. *Int J Impot Res* 2018; 30(2): 88–94. doi: 10.1038/s41443-017-0005-7
14. Lee YJ, Kim HY, Kim YS, Seol GH, Lee CM. Lancemaside A, a major triterpene saponin of *Codonopsis lanceolata*, enhances regulation of nitric oxide synthesis via eNOS activation. *BMC Complement Altern Med* 2019; 19(1): 73. doi: 10.1186/s12906-019-2484-4
15. Vilahur G, Padró T, Casaní L, Mendieta G, López JA, Streitenberger S, et al. Polyphenol-enriched diet prevents coronary endothelial dysfunction by activating the Akt/eNOS pathway. *Rev Esp Cardiol (Engl Ed)* 2014; 67(12): 1004–11. doi: 10.1016/j.rec.2014.04.014
16. Xu Y, Zhang H, Bai X, Yuan J, Wang Y, Liu J, et al. Botanical drugs for treating erectile dysfunction: clinical evidence. *Front Pharmacol* 2023; 14: 1101949. doi: 10.3389/fphar.2023.1101949
17. Renda CR, Leri F. The anxiogenic drug yohimbine is a reinforcer in male and female rats. *Neuropsychopharmacology* 2024; 49(5): 894–903. doi: 10.1038/s41386-023-01780-9
18. Aydın N, Demir B, Akdağ A, Gökmen S, Sayaslan A, Bayraç AT, et al. Accelerated breeding strategies for biochemical marker-assisted backcross breeding and mapping population development in bread wheat (*Triticum aestivum* L.). *Euphytica* 2024; 220(5): 360. doi: 10.1007/s10681-024-03260-0
19. Milićević N, Mazzaro N, Bruin C, Wils L, Brink JV, Asbroek AA, et al. Rev-Erba and photoreceptor outer segments modulate the circadian clock in retinal pigment epithelial cells. *Sci Rep* 2019; 9(1): 19725. doi: 10.1038/s41598-019-56118-3
20. Schmid KT, Höllbacher B, Cruceanu C, Böttcher Y, Lickert H, Binder EB, et al. scPower accelerates and optimizes the design of multi-sample single-cell transcriptomic studies. *Nat Commun* 2021; 12(1): 6623. doi: 10.1038/s41467-021-26832-6
21. National Research Council (US) Committee for the Update of the Guide for the Care and Use of Laboratory Animals. *Guide for the care and use of laboratory animals*. 8th ed. Washington, DC: National Academies Press; 2011. doi: 10.17226/12910

*Christabel A. Omogiade

Department of Medical Laboratory Science
School of Basic Medical Sciences
College of Medical Sciences
University of Benin
Benin City, Nigeria
Email: adaegbus29@gmail.com