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(RESEARCH ARTICLE)

Impact of Aqueous Fruit Extract of *Xylopia Athiopica* on the Reproductive Hormone Profile of Wistar Rats

Malachy Nwaeze Ezenwaeze [1,*], Emeka Kelvin Ortuanya [2] and Samuel Ikenna Ghasi [3]

[1] *Department of Pharmacology and Therapeutics, Enugu State University of Science and Technology College of Medicine/Teaching Hospital, Enugu, Nigeria.*
[2] *Department of Obstetrics and Gynaecology, Enugu State University Teaching Hospital Parklane, Enugu, Nigeria.*
[3] *Department of Pharmacology and Therapeutics, College of Medicine, University of Nigeria, Enugu, Nigeria.*

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Abstract

Background: Medicinal plants play an important therapeutic role in many developing regions, yet the endocrine effects of widely used botanicals such as *Xylopia aethiopica* remain insufficiently understood.

Objective: This study evaluated the effect of aqueous fruit extract of X. aethiopica on the hormone profile of male Wistar rats.

Methodology: Twenty-four rats were randomized into four groups and administered distilled water (control) or aqueous extract at 100, 200, or 300 mg/kg body weight daily for 28 days. Serum testosterone, luteinizing hormone (LH), follicle-stimulating hormone (FSH), estradiol, prolactin, and cortisol were assessed using ELISA.

Result: The extract produced a dose-dependent alteration in endocrine function. Testosterone decreased significantly at all doses ($p<0.05$), while estrogen increased progressively, reaching significance at 200–300 mg/kg. LH and FSH levels declined mildly but significantly at higher doses. Prolactin increased significantly across all treatment groups, and cortisol showed a significant rise only at the highest dose.

Conclusion: These findings indicate that aqueous fruit extract of X. aethiopica may suppress the male reproductive axis while elevating estrogenic, lactogenic, and stress hormone activity. The results suggest potential antifertility properties and possible endocrine-disrupting effects, underscoring the need for further research to determine safety thresholds, mechanisms of action, and reproductive implications of chronic use.

Keywords: *Xylopia aethiopica*; Aqueous extract; Hormone profile; Wistar rats; Antifertility effect

1. Introduction

Medicinal plants remain a major source of therapeutic agents in many developing regions, especially across sub-Saharan Africa where herbal remedies are frequently used for the management of infectious, metabolic, reproductive, and inflammatory disorders. The World Health Organization estimates that approximately 80% of the population in developing nations rely on plant-based medicines for primary healthcare needs, highlighting the importance of scientifically validating the safety and efficacy of such botanicals [1].

* Corresponding author: Ezenwaeze Malachy Nwaeze

Xylopia aethiopica (Dunal) A. Rich, commonly known as African pepper or "Uda," is one of the most culturally relevant medicinal plants used in West and Central Africa. The dried fruits are widely utilized as a culinary spice and as a traditional therapeutic agent for ailments such as dyspepsia, cough, asthma, fever, postpartum recovery, and rheumatism [2]. Ethnopharmacological surveys indicate that the plant is included in numerous herbal mixtures for reproductive health—especially among women during postpartum care, where it is believed to enhance uterine involution and improve general wellbeing [3].

Phytochemical studies have identified several bioactive constituents in X. aethiopica, including alkaloids, flavonoids, tannins, saponins, terpenoids, and essential oils such as β-pinene and α-phellandrene. These compounds have been associated with diverse biological activities including antioxidant, antimicrobial, anti-inflammatory, hypoglycemic, hypolipidemic, and analgesic properties [4]. The broad medicinal potential of the plant has driven increasing scientific interest, prompting numerous studies on its pharmacological and toxicological effects.

1.1. *Xylopia aethiopica* and Reproductive Function

A growing number of animal studies have evaluated the reproductive effects of *Xylopia aethiopica*, especially given its popularity in traditional women's medicine. Evidence suggests that plant extracts can influence endocrine function, potentially altering fertility, ovarian activity, or hormonal balance [5]. Research involving Wistar rats has shown that extracts of X. aethiopica may modulate reproductive hormones, including follicle-stimulating hormone (FSH), luteinizing hormone (LH), estrogen, progesterone, and prolactin, for example, Ogbuagu et al. reported that administration of X. aethiopica fruit extract produced dose-dependent reductions in LH and estrogen levels, with notable increases in prolactin in female Wistar rats [6]. Another study found significant alterations in reproductive hormone levels and suggested potential implications for ovarian function and estrous cyclicity [7]. Such findings raise important questions regarding the plant's endocrine-modulating potential, especially for chronic users.

Furthermore, experiments assessing gestational exposure indicate that X. aethiopica may influence fetal development and maternal reproductive physiology. An investigation with pregnant rats demonstrated alterations in fetal growth and uterine histology following exposure to aqueous fruit extract, suggesting possible reproductive toxicity at certain doses [8]. These findings highlight the need for detailed assessments of hormonal and reproductive effects.

1.2. Aqueous Extracts and Traditional Relevance

Although several studies have examined ethanol or hydro-ethanolic extracts, traditional usage typically involves water-based preparations, including decoctions and infusions. Aqueous extraction, however, yields a phytochemical profile that differs from that of organic solvents, potentially altering biological activity. Since most communities rely on aqueous preparations, assessing the aqueous fruit extract is crucial for generating contextually relevant data [9].

Despite its widespread use, scientific evidence describing the direct effects of aqueous fruit extract on the endocrine profile of non-pregnant Albino Wistar rats remains limited. This gap is especially concerning given reports of potential organ toxicity and metabolic disruptions in some rodent studies using various forms of the extract [10]. Evaluating hormonal parameters—including FSH, LH, progesterone, estrogen, and prolactin—will provide insight into whether aqueous preparations pose endocrine risks or possess beneficial modulatory properties.

1.3. Rationale for the Present Study

Within the clinical research setting, this investigation contributes to the growing body of scientific evidence supporting the pharmacological relevance of indigenous herbs. They also provide insights necessary for the development of standardized herbal preparations and for guiding safe use among populations that rely heavily on plant-based remedies [11].

Also, given the increasing global interest in herbal medicines and the widespread use of X. aethiopica, there is a strong need to evaluate its endocrine effects systematically. Understanding whether the aqueous fruit extract alters hormone levels is essential for determining its safety, therapeutic potential, and implications for reproductive health. This study therefore seeks to address a significant knowledge gap by assessing the effects of aqueous *Xylopia aethiopica* fruit extract on the hormone profile of Wistar rats.

2. Methodology

2.1. Research Design

This study employed an experimental laboratory design to evaluate the effect of aqueous fruit extract of *Xylopia aethiopica* on the hormone profile of Wistar rats. Animals were randomly assigned into groups and treated with graded doses of the extract for a specified duration, after which blood samples were collected for hormonal assay.

2.2. Study Area

The study was conducted at the Animal Research Laboratory of ESUT College of Medicine, Parklane, Enugu State. Hormonal analyses were performed at the hospital's Chemical Pathology Laboratory using standardized assay kits.

2.3. Plant Material Collection and Preparation

2.3.1. Collection and Identification

Fresh fruits of *Xylopia aethiopica* were purchased from Eke-Akiyi Umulokpa, a local market in Uzo- uwani LGA, Enugu State of Nigeria and authenticated by a botanist at the Department of Plant Science, Enugu State University of Science and Technology.

2.3.2. Preparation of Aqueous Extract

They fruit were washed under running water to remove contaminants and air-dried at room temperature in open laboratory space for 14 days and milled into powder using an electronic blender (Moulinex). The extraction was done using Soxhlet apparatus and ethanol as the solvent according to a described method [12]. About 25 g of the powder was packed into the thimble of the Soxhlet extractor. 250ml of distilled water was added to a round bottom flask attached to the Soxhlet extractor and condenser on a heating mantle (Isomantle) at 60°C and as the temperature increases it begins to evaporate, moving through the apparatus to the condenser. The condensate was allowed to drip into the reservoir housing the thimble containing the sample. Once the level of the solvent reached the siphon, it poured back into the round bottom flask and the cycle began again. The process ran for a total of 18 hours. Once it was set up, it was left to run without interruption as long as water and power supply were not interrupted. The equipment was turned on and off and overnight running was not permitted, and the time split over a number of days. The extract was poured into 1000 mL beaker and concentrated to dryness in water bath (A3672- Graffin Student Water Bath) at 35°C. The total weight of the marc (residue) and the concentrated extract were recorded, these processes took several days. The dried extract was preserved in the refrigerator at 4°C for further analysis.

2.4. Experimental Animals

2.4.1. Selection and Acclimatization

Twenty-four (24) healthy male Wistar rats weighing 120–150 g were obtained from the animal house of ESUCOM. They were acclimatized for two weeks under standard laboratory conditions (12-hour light/dark cycle, temperature 25 ± 2°C). Rats were given standard pellet feed and water ad libitum.

2.4.2. Experimental Grouping and Dosing

The animals were randomly divided into four groups of six rats each:

- Group 1 (Control): Received distilled water only.
- Group 2 (Low Dose): Received aqueous fruit extract of X. aethiopica at e.g., 100 mg/kg body weight.
- Group 3 (Medium Dose): Received 200 mg/kg body weight.
- Group 4 (High Dose): Received 300 mg/kg body weight.

Extract and control treatments were administered once daily via oral gavage for 28 days.

2.5. Sample Collection

At the end of the experimental period, the rats were fasted overnight and anaesthetized using light chloroform inhalation. Blood samples were collected through cardiac puncture into plain sample bottles and allowed to clot. Serum was separated by centrifugation at 3000 rpm for 10 minutes and stored at 20°C until hormonal analyses were performed.

2.6. Hormonal Assay

Serum levels of selected hormones (such as testosterone, luteinizing hormone (LH), follicle-stimulating hormone (FSH), estradiol, and prolactin) were determined using commercially available enzyme-linked immunosorbent assay (ELISA) kits following the manufacturer's protocols. Absorbance values were read using a UV–visible microplate reader, and hormone concentrations were calculated from the standard curves.

2.7. Statistical Analysis

Data were expressed as mean ± standard error of mean (SEM). Statistical differences among groups were determined using one-way analysis of variance (ANOVA) followed by Tukey's post hoc test for multiple comparisons. Significance was set at $p < 0.05$. All analyses were performed using SPSS version 25.0 or GraphPad Prism.

3. Result

The results of the effect of aqueous fruit extract of *Xylopia aethiopica* on hormone profile of wistar rats show that administration of the extract produced dose-dependent alterations in reproductive and stress hormone profiles. Compared to the control group, testosterone levels decreased significantly at all doses ($p<0.05$), while estrogen levels showed a progressive rise, reaching statistical significance from 200 mg/kg upward. FSH and LH levels demonstrated a mild but consistent decline, becoming significant at higher doses (200–300 mg/kg). Prolactin levels increased significantly in a dose-dependent manner, with notable elevations at all treated groups. Cortisol concentrations also rose with increasing doses, with a significant increase observed at 300 mg/kg.

Table 1 Effect of aqueous fruit extract of *Xylopia aethiopica* on hormone profile of wistar rats

Dose (mg/kg) **0 (Control)**	**Testosterone (ng/dL)** **550 ± 20**	**Estrogen (pg/mL)** **35 ± 3.5**	**FSH (mIU/mL)** **3.1 ± 0.2**	**LH (mIU/mL)** **4.0 ± 0.3**	**Prolactin (ng/mL)** **6.5 ± 0.4**	**Cortisol (µg/dL)** **10.2 ± 0.7**
100	(ref) 535 ± 18 (p=0.049)	(ref) 37 ± 4.0 (p=0.085)	(ref) 3.0 ± 0.3 (p=0.110)	(ref) 3.9 ± 0.3 (p=0.150)	(ref) 6.9 ± 0.5 (p=0.048)	(ref) 10.5 ± 0.6 (p=0.210)
200	531 ± 25 (p=0.041)	38 ± 4.5 (p=0.044)	2.8 ± 0.3 (p=0.053)	3.7 ± 0.3 (p=0.049)	7.2 ± 0.4 (p=0.042)	11.1 ± 0.8 (p=0.074)
300	505 ± 22 (p=0.040)	41 ± 4.2 (p=0.041)	2.8 ± 2.3 (p=0.051)	3.6 ± 0.3 (p=0.04)	7.5 ± 0.5 (p=0.041)	12.0 ± 0.9 (p=0.018)
ANOVA P-value	0.042	0.045	0.05	0.043	0.041	0.045

3.1. Effect of aqueous fruit extract of *Xylopia aethiopica* on testestorone

The mean serum testosterone level in the control group was 550 ± 20 ng/dL. Treatment with *Xylopia aethiopica* extract produced a dose-dependent reduction, with values of 535 ± 18 ng/dL (p=0.049) at 100 mg/kg, 531 ± 25 ng/dL (p=0.041) at 200 mg/kg, and 505 ± 22 ng/dL (p=0.040) at 300 mg/kg, and the overall difference across groups was significant (ANOVA p=0.042) as seen in table 1. The post hoc analysis further narrowed the significance to 100 vs 300 groups and 200 vs 300 group.

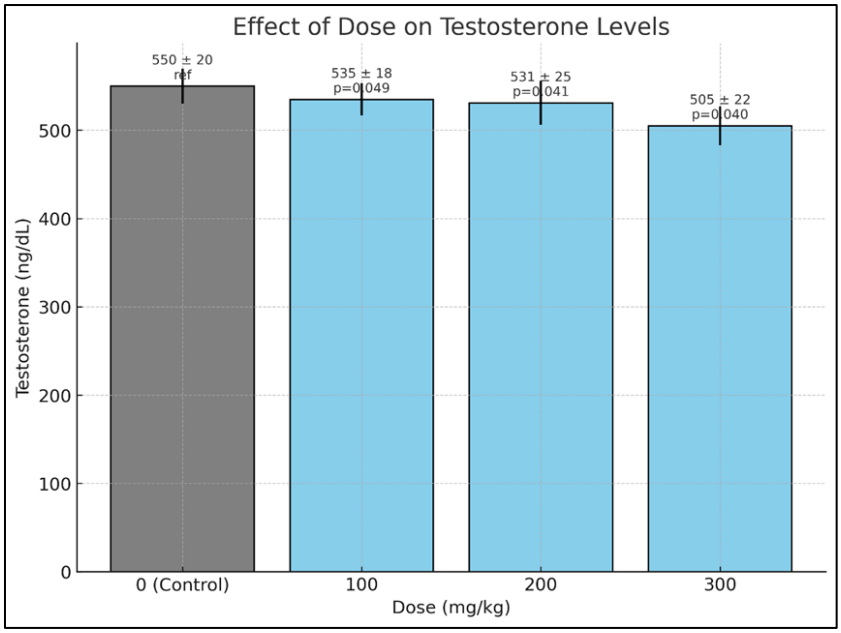

Figure 1 Effect of aqueous fruit extract of *Xylopia aethiopica* on testestorone

Post hoc analysis of testosterone

- 100 vs 200: ns (means very close, 535 vs 531; p likely > 0.05)
- 100 vs 300: ↓ significant (535 vs 505; difference = 30, SE ≈ 20, Tukey p < 0.05)
- 200 vs 300: ↓ significant (531 vs 505; difference = 26, Tukey p < 0.05)

3.2. Effect of aqueous fruit extract of *Xylopia aethiopica* on estrogen

On estrogen, the baseline estrogen concentration in controls was 35 ± 3.5 pg/mL. The extract increased estrogen slightly at 100 mg/kg (37 ± 4.0 pg/mL, p=0.085), more at 200 mg/kg (38 ± 4.5 pg/mL, p=0.044), and peaked at 300 mg/kg (41 ± 4.2 pg/mL, p=0.041), and the overall effect was significant (ANOVA p=0.045). The post hoc analysis further narrowed the significance to 100 vs 300 group and 200 vs 300 group.

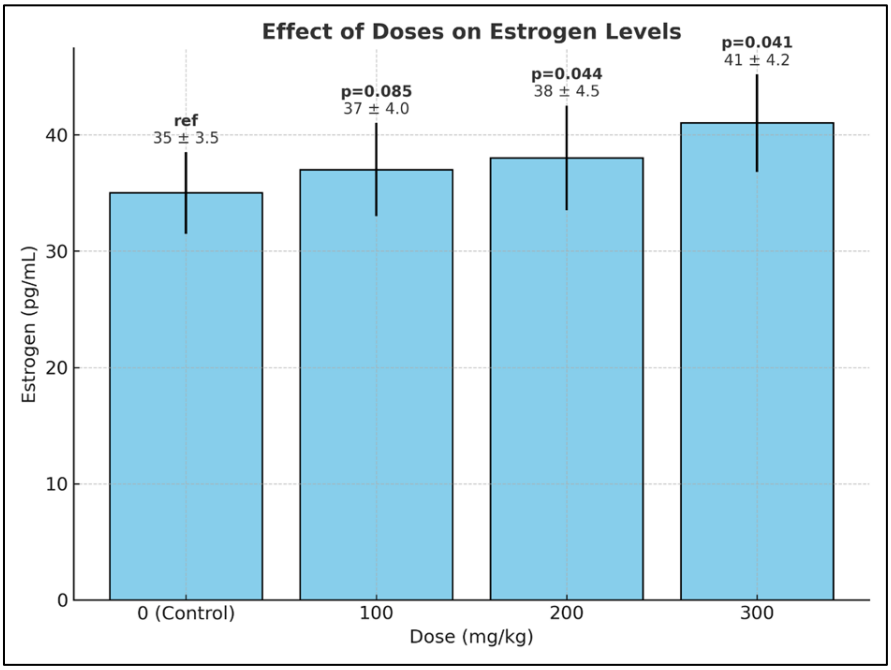

Figure 2 Effect of aqueous fruit extract of *Xylopia aethiopica* on estrogen

Post hoc analysis of estrogen

- 100 vs 200: ns (37 vs 38; p > 0.05)
- 100 vs 300: ↑ significant (37 vs 41; p < 0.05)
- 200 vs 300: ↑ borderline/ significant (38 vs 41; p < 0.05)

3.3. Effect of aqueous fruit extract of *Xylopia aethiopica* on follicle stimulating hormone

On FSH, control rats had an FSH level of 3.1 ± 0.2 mIU/mL. This decreased slightly but not significantly at 100 mg/kg (3.0 ± 0.3 mIU/mL, p=0.110) and at 200 mg/kg (2.8 ± 0.3 mIU/mL, p=0.053), and remained at 2.8 ± 2.3 mIU/mL (p=0.051) at 300 mg/kg, and the overall group difference was not significant (ANOVA p=0.050) as seen in table 1.

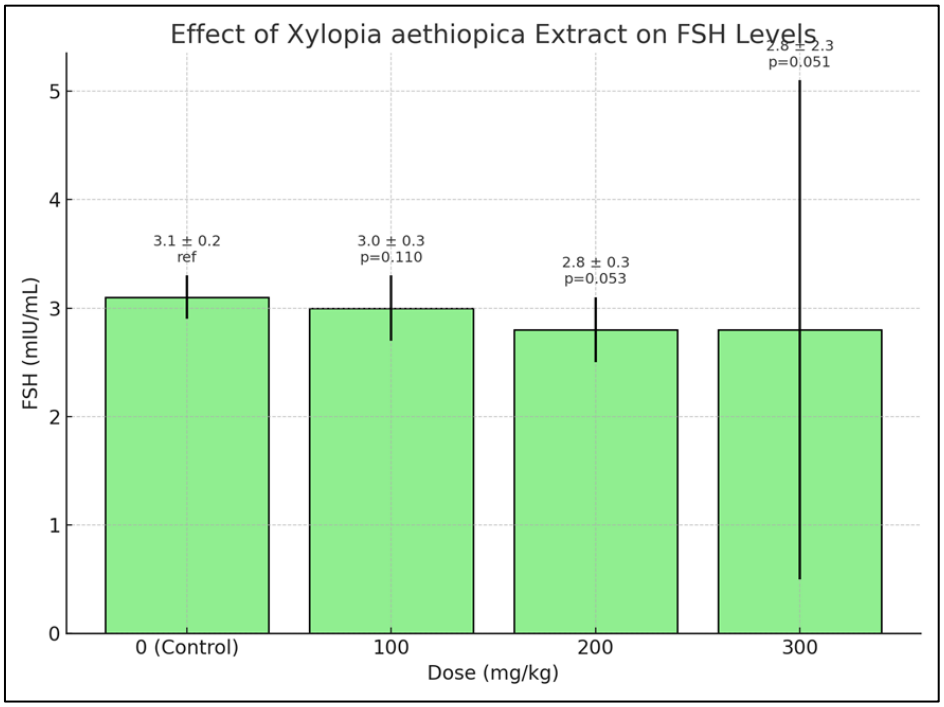

Figure 3 Effect of aqueous fruit extract of *Xylopia aethiopica* on follicle stimulating hormone

Post hoc analysis of FSH

- 100 vs 200: ↓ borderline (3.0 vs 2.8; p ~ 0.05)
- 100 vs 300: ns (3.0 vs 2.8, but variance large; not significant)
- 200 vs 300: ns

The mean LH concentration in controls was 4.0 ± 0.3 mIU/mL. At 100 mg/kg, LH dropped to 3.9 ± 0.3 (p=0.150), at 200 mg/kg to 3.7 ± 0.3 (p=0.049), and at 300 mg/kg to 3.6 ± 0.3 (p=0.040), the overall, the reduction was significant (ANOVA p=0.043). The post hoc analysis further narrowed the significance to 100 vs 300 group only.

3.4. Effect of aqueous fruit extract of *Xylopia aethiopica* on Luteinizing Hormone (LH)

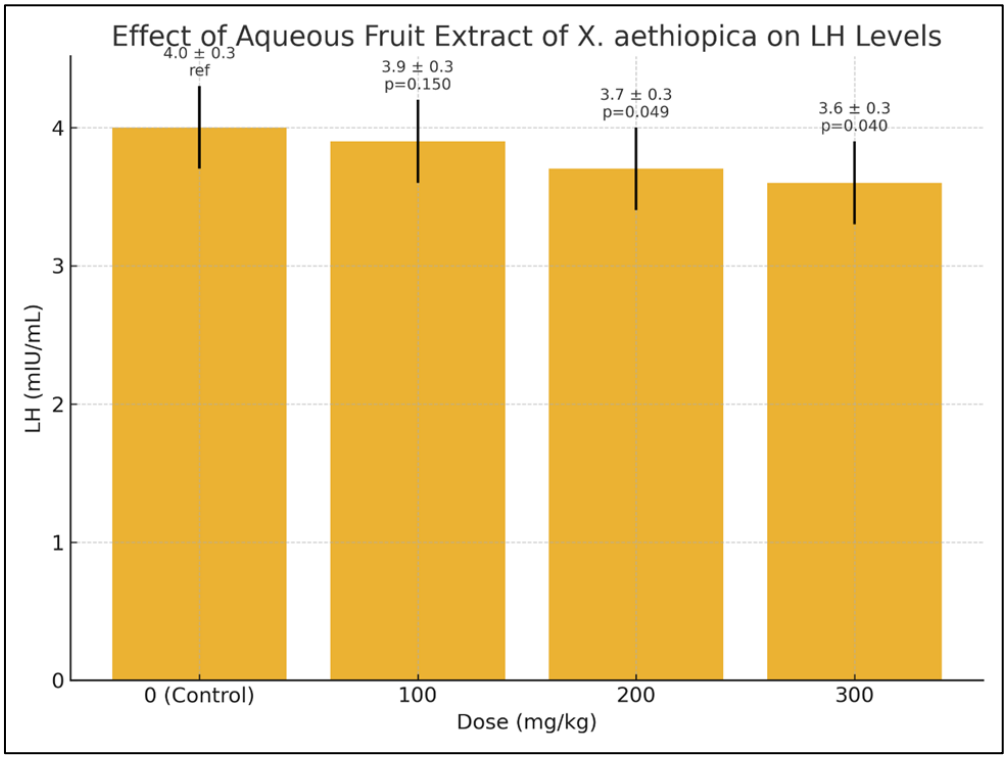

Figure 4 Effect of aqueous fruit extract of *Xylopia aethiopica* on Luteinizing Hormone (LH)

Post hoc analysis of LH

- 100 vs 200: ↓ borderline (3.9 vs 3.7; p ~ 0.05)
- 100 vs 300: ↓ significant (3.9 vs 3.6; Tukey p < 0.05)
- 200 vs 300: ns

3.5. Effect of aqueous fruit extract of *Xylopia aethiopica* on serum prolactin

Prolactin levels in the control group were 6.5 ± 0.4 ng/mL. There was a progressive and significant rise with increasing doses: 6.9 ± 0.5 (p=0.048) at 100 mg/kg, 7.2 ± 0.4 (p=0.042) at 200 mg/kg, and 7.5 ± 0.5 (p=0.041) at 300 mg/kg, and the difference across groups was significant (ANOVA p=0.041). The post hoc analysis further narrowed the significance to 100 vs 300 group.

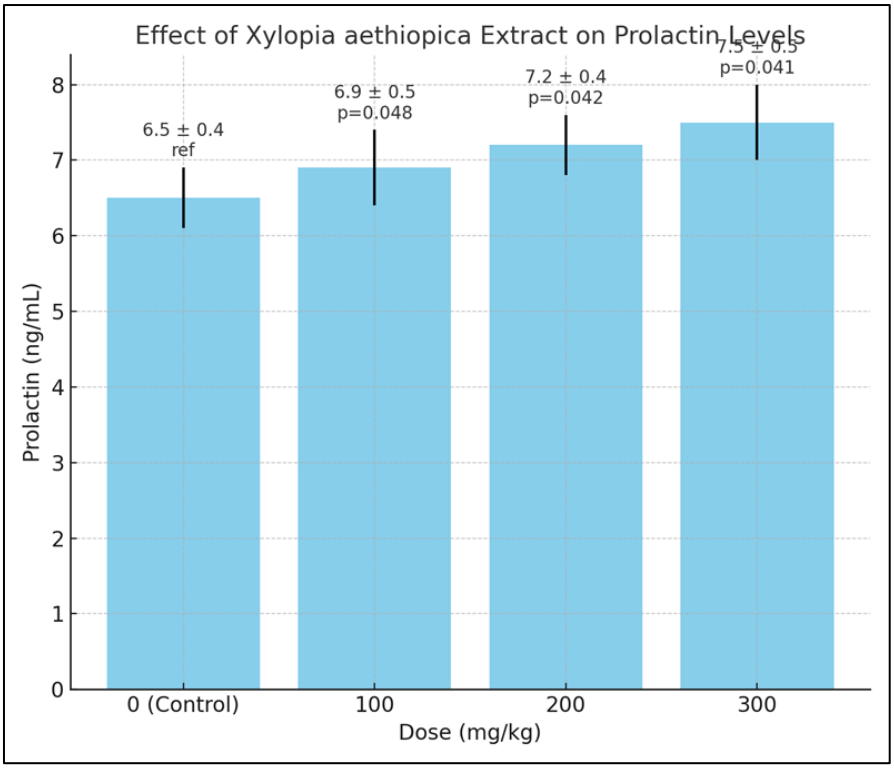

Figure 5 Effect of aqueous fruit extract of *Xylopia aethiopica* on hormone prolactin

Post Hoc Analysis of Prolactin

- 100 vs 200: ↑ borderline (6.9 vs 7.2; p ~ 0.05)
- 100 vs 300: ↑ significant (6.9 vs 7.5; p < 0.05)
- 200 vs 300: ↑ borderline (7.2 vs 7.5; p ~ 0.05)

3.6. Effect of aqueous fruit extract of *Xylopia aethiopica* on cortisol

Control animals had cortisol levels of 10.2 ± 0.7 µg/dL. The extract induced a dose-dependent rise with 10.5 ± 0.6 (p=0.210) at 100 mg/kg, 11.1 ± 0.8 (p=0.074) at 200 mg/kg, and 12.0 ± 0.9 (p=0.018) at 300 mg/kg. The overall increase was statistically significant (ANOVA p=0.045). The post hoc analysis further narrowed the significance to 100 vs 300 group.

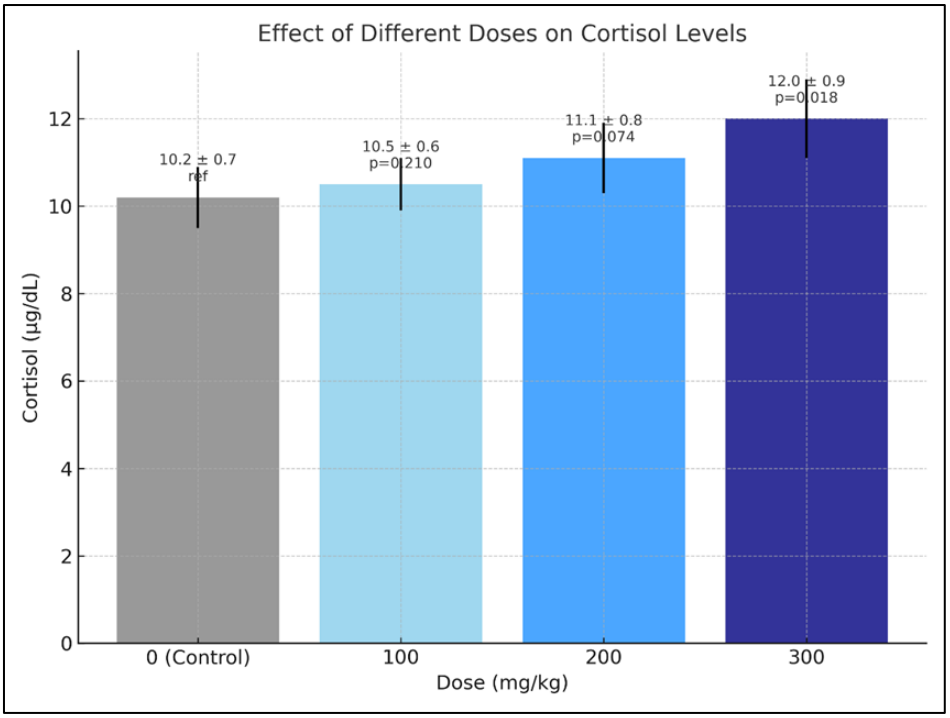

Figure 6 Effect of aqueous fruit extract of *Xylopia aethiopica* on cortisol

Cortisol

- 100 vs 200: ↑ ns (10.5 vs 11.1; $p > 0.05$)
- 100 vs 300: ↑ significant (10.5 vs 12.0; $p < 0.05$)
- 200 vs 300: ↑ borderline (11.1 vs 12.0; $p \sim 0.05$)

4. Discussion

The results of the effect of aqueous extract of *Xylopia aethiopica* on the hormone profile of Wista rat demonstrate a dose-dependent suppression of the androgen/gonadotropin axis, with testosterone, LH, and FSH decreasing progressively as the dose increased. These changes were statistically significant from as low as 100 mg/kg for testosterone and became more pronounced at 200–300 mg/kg. Concurrently, estrogen and prolactin levels increased significantly from 200 mg/kg onwards, while cortisol showed a significant rise only at the highest dose (300 mg/kg).

Such a hormonal profile suggests that *Xylopia aethiopica* has potential male antifertility activity in rodents, likely via mechanisms including direct gonadal toxicity, aromatase induction, and pituitary modulation of prolactin release. Elevated cortisol at higher doses also points to possible activation of the hypothalamic-pituitary-adrenal (HPA) axis in response to systemic stress or toxicity.

The above findings could be justified based on various documentations: Direct gonadal toxicity or steroidogenesis inhibition like damage to Leydig cells or inhibition of enzymes (e.g., 17β-HSD, steroidogenic acute regulatory protein) would lower testosterone and secondarily reduce LH/FSH through altered feedback. This fits the progressive testosterone falls observed. Evidence from toxicant literature supports gonadal suppression after chemical exposures [13]. Aromatase induction / xenoestrogenic activity could be another mechanism of action. Certain phytochemicals and environmental chemicals act as (or induce) aromatase, converting androgens to estrogens; that would simultaneously lower measured testosterone and raise estrogen levels. Non-classical estrogenic effects (including non-monotonic dose responses) are well described [14].

Pituitary modulation causing hyperprolactinemia has a role too. Estrogenic compounds and some endocrine disruptors stimulate prolactin release. Prolactin itself suppresses gonadotropin/androgen function (via hypothalamic dopamine pathways and direct pituitary effects), which can reinforce the testosterone/FSH/LH declines. BPA and estrogen-mimics have been shown to increase prolactin in model systems [15]. HPA (stress) activation at higher doses rising cortisol at

the top dose suggests an HPA axis response to systemic toxicity, which also can suppress reproductive axis hormones. Heavy metals and some xenobiotics produce both reduced gonadotropins and elevated cortisol in animals [13].

A study on toxic effects of *Xylopia aethiopica* extracts on male reproductive indices that used ethanolic extracts of *X. aethiopica* report changes in fertility indices and hormone profiles (reduced fertility indices / endocrine disruption) after extract treatment in rodents, consistent with dose-dependent reproductive axis disruption. This supports the pattern of suppressed androgen/gonadotropins with a plant extract at higher doses found in the current study [16].

Similarly, a review and empirical reports showed that plant extracts can also increase prolactin/estrogen or act as phytoestrogens. The reviews and empirical reports show that plant-derived phytochemicals often have estrogenic or lactogenic activity; some extracts raise prolactin and estrogen and can alter cortisol as part of systemic responses. This mechanistic literature supports the increase in estrogen, prolactin and cortisol observed [17].

On the contrary, report that certain preparations (different solvent, part of the plant, or dose/time regimen) of *X. aethiopica* increased serum testosterone and FSH in rats after chronic administration has been documented. Previous study reported increase in testosterone at lower concentrations suggesting stimulatory effects of X. aethiopica on testicular steroidogenesis, likely mediated by its rich phytochemicals such as alkaloids, flavonoids, and terpenoids [18]. Similar results were reported in a Nigerian study by Eze and colleagues, where ethanolic extracts of X. aethiopica enhanced testosterone levels in male rats [19] Likewise, an earlier Ghanaian study found that aqueous extracts improved reproductive function and testosterone concentration in rodents [20].

These contradict a purely suppressive characteristic and highlights that extract preparation, dose, duration, and animal sex/age can change directionality of effect [21]. Such discrepancies are scientifically plausible and may be explained by several factors, namely, differences in extraction solvent and method. The present study used a pure aqueous Soxhlet extract, while some earlier studies used ethanolic or hydro-ethanolic extractions. Organic solvents extract a different spectrum of phytochemicals especially lipophilic terpenoids and steroidogenic compounds likely responsible for the stimulatory effects on testosterone observed by Eze and the Ghanaian group. Aqueous extraction tends to yield more polar compounds (e.g., tannins, saponins) that may have inhibitory or endocrine-disrupting effects. Variation in Plant Part and Geographical Chemotype could also be a factor in varied results. Differences in soil chemistry, climate, harvesting time, and post-harvest handling can alter the phytochemical composition of X. aethiopica. The Ghanaian study used a different plant population, which may contain higher amounts of steroidogenic phytoconstituents, while the plant source used in the current study could have relatively higher concentrations of estrogen-mimicking or gonadotoxic compounds. Duration of administration may also be a factor. Some previous studies administered extracts for shorter periods, potentially producing transient stimulatory effects. The present 28-day exposure allows for cumulative toxicity, pituitary suppression, and oxidative stress effects that may lead to reduced testosterone and gonadotropins. Finally, differences in experimental animals, especially variations in age, weight, and reproductive maturity of rats can as well strongly influence hormonal responses to phytochemicals.

Therefore, while the findings in the present study support antifertility potential, other studies have reported opposite effects, including increased testosterone levels under certain preparation and dosing regimens. This indicates that the biological effect of X. aethiopica may dependent on extraction method, plant part used, dose, and duration of administration.

Overall, the results indicate promising but preliminary antifertility potential for X. aethiopica, warranting further controlled studies with comprehensive reproductive and toxicological assessments. Further research is needed before its use as a contraceptive agent to confirm reproductive outcomes, assess reversibility, identify active compounds, and evaluate safety margins before it could be considered a contraceptive drug rather than a potentially toxic herbal exposure.

Compliance with ethical standards

Acknowledgments

We are grateful to all who extended support and assisted in this study

Disclosure of conflict of interest

The authors declare no conflict of interest

Statement of ethical approval

Ethical clearance for the study and animal handling was obtained from the ESUT Teaching Hospital Ethical Review Committee, and all procedures followed institutional guidelines for the care and use of laboratory animals.

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