

Original Research Article

Alterations in Female Reproductive Hormones of Wistar Rats sequel to the Administration of *Xylopi* *aethiopic* Fruit

ABSTRACT

Aim: This study was designed to examine the effect of *Xylopi* *aethiopic* fruit on the reproductive hormones of female Wistar rats.

Methodology: The fruits of *Xylopi* *aethiopic* were air-dried and extracted by Soxhlet extractor using ethanol as solvent. The lethal dose of the plant extract was assessed by standard method. Thirty adult female Wistar rats were grouped into 5 of 6 rats each. Animals in groups 1, 2, 3, and 4 were exposed to 130, 259, 389 and 518 mg/kg body weight of *X. aethiopic* fruit extract respectively, while those in group 5 received normal animal feeds and water only. The administration was done once daily for 28 days via oral route. Reproductive hormones were assay using ELISA techniques.

Results: A non-significant increase was observed in the blood concentration of follicle stimulating hormone (FSH) when animals treated with 130 mg/kg body weight of *Xylopi* *aethiopic* extract were compared with those in the control group. Increase in the dose of *Xylopi* *aethiopic* extract resulted in a decrease in serum FSH levels. Administration of the extract for 28 days led to a dose-dependent decline in the blood level of luteinizing hormone (LH). The result of this study indicates the extract decreased serum level of progesterone in female rats at low doses of 130 mg/kg and 259 mg/kg when compared with those in the control group. However, increasing the dosage of the extract increases the serum progesterone concentrations. Administration of *Xylopi* *aethiopic* extract to animals for 28 days led to a dose-dependent decrease in the serum level of estrogen. This decrease was only significant ($P < 0.05$) when the estrogen levels of animals treated with 389 mg/kg and 518 mg/kg of *Xylopi* *aethiopic* extract were respectively compared with those in the control group. Conversely, *Xylopi* *aethiopic* extract increases serum levels of prolactin with respect to dosage.

Conclusion: The impact of *Xylopi* *aethiopic* extract on female reproductive hormones observed in this study showed that the extract might be a potent contraceptive. Contraceptives of plant origin should be generally acceptable because they are less expensive with minimum adverse effects than synthetic agents.

Keywords: Contraceptive; female reproductive hormones; infertility; *Xylopi* *aethiopic* fruit

1. INTRODUCTION

Xylopi *aethiopic* has a great patronage in both nutrition and ethnomedicine. The plant which also known as African Negro pepper, is popular among traditional medicine practitioners and traditional birth attendants (TBA) who utilize the fruit preparations to cause the discharge of placental after a woman has giving birth [6]. A preparation of the stem bark or fruit is helpful in the management of bronchitis, stomach aches, asthma, and dysenteric conditions [1]. The seed

extract is helpful as a vermifuge for roundworms [2]. Several postnatal women eat the aqueous preparation of the fruit for its perceived antiseptic properties. Some of the women have been reported to sometimes come to the hospitals with characteristics which suggest complications in organ [3]. Medicinal plant extracts with a therapeutic property has the tendency of wrong prescription and sometimes, overdosed. The fact that *Xylopi* *aethiopic* is a natural product does not automatically confers on it safety and might be risky to its consumers.

Comment [AaM1]: potential

Comment [AaM2]: might

Chemical ingredients of the plant are perceived to be useful in preventing and managing cancerous tumors [4]. *Xylopi*a *aethi*o*pica* fruit is known to have alkaloids, terpenoids, flavonoids, and organic oils [5,6].



*Xylopi*a *aethi*o*pica* is characterized with numerous chemical components with various medicinal potentials [8]. The chemical components of this plant have been investigated to include saponins, sterols, carbohydrates, glycosides, mucilage, acidic compounds, tannins, balsams, cardiac glycosides, volatile aromatic oils, phenols [9,10], alkaloids, rutin and fixed oils [11,12]. The plant has also been known to contain vitamins such as vitamin A, vitamin B, vitamin C, vitamin D, and vitamin E, and proteins as well as several minerals such as copper, manganese and zinc [10,12]. The impact of the fruit on body weight and glucose concentration [13] and lipid profile [14] of animals has been reported [13]. The fruit has also been reported to induce hepatotoxicity [15], renal toxicity [16] as well as oxidative stress [17]. Recently, Ogbuagu et al. [18] reported that the fruit extract of *Xylopi*a *aethi*o*pica* adversely perturbed sperm qualities in male Wistar rats. This study was therefore aimed at investigating its effect on the reproductive hormones of female Wistar rats.

2. MATERIALS AND METHODS

2.1 Collection and Authentication of Plant Materials

The fruits of *Xylopi*a *aethi*o*pica* were sourced from a market in Aba, Abia State. They were identified and authenticated by Prof. Margaret Basse

2.2 Extraction of Plant Materials

Extraction of the plant was carried out in the Post-graduate Laboratory of Department of Pharmacognosy and Natural Medicine, Faculty of Pharmacy, University of Uyo, Nigeria. It was extracted based on the outlined method in Ogbuagu et al. [7]. The fruits were rinsed under flowing tap water to eliminate contaminants and air-dried. The plant material was milled by laboratory blender. The pulverized plant material was macerated in 250 mL of 99.8% ethanol (Sigma Aldrich) contained in a flask attached to a Soxhlet extractor coupled with condenser and heating mantle (Isomantle). It was then poured into the sample holder (thimble) and inserted in the apparatus. The side arm is lagged with glass wool. The mixture was heated using the heating mantle (Isomantle) at 60 °C and as the temperature rises it starts to evaporate, going via the extractor to the condenser. The condensate dripped into the reservoir housing the thimble. As soon as the solvent gets to the siphon it emptied itself into the flask and the process repeats itself. The process goes on until it is exhaustively extracted. The process runs for a total of 13 hours. As soon as it was set up, it was allowed to run without interruption as long as water and power supply were not interrupted. The apparatus was switched on and off and overnight running was not allowed, and the time for the complete process split over some 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 noted. Several days was spent on the entire process. The evaporated extract was kept in the refrigerator until when the need for it arise.

2.3 Determination of Median Lethal Dose (LD₅₀)

The median lethal dose (LD₅₀) of the extract was determined using albino mice according to the

method described by Airaodion et al. [19]. This method involves two phases:

In Phase one, five groups containing five mice each weighing between 20 g and 27g were fasted for 18 hours. They were respectively treated with 1000 mg/kg, 2000 mg/kg, 3000 mg/kg, 4000 mg/kg and 5000 mg/kg body weight via intraperitoneal (i.p) route and were monitored for visible signs of toxicity and mortality for 24 hours. A dosage of 1000 mg/kg recorded 0% mortality while 2000 mg/kg, 3000 mg/kg 4000 mg/kg and 5000 mg/kg recorded 100% mortality within 24 hours. Based on the value of phase one, phase two was conducted.

In Phase two, twenty-five albino mice weighing between 20 and 27g were grouped into 5 of 5 mice per group and were fasted for 18 hours. Each group was administered 1200 mg/kg, 1400 mg/kg 1600 mg/kg, 1800 mg/kg and 2000 mg/kg body weight intraperitoneally (i.p) and was observed for physical signs of toxicity and mortality within 24 hours. 1200 mg/kg recorded 0% mortality while 1400 mg/kg, 1600 mg/kg, 1800 mg/kg and 2000 mg/kg recorded 100% mortality within 24 hours. The LD_{50} was computed as geometrical means of the maximum dose yielding 0% mortality (a) and the minimum dose yielding 100% death (b).

$$LD_{50} = \sqrt{ab}$$

2.4 Experimental Design

Thirty female Wistar rats used in this study were purchased from the University of Uyo, Nigeria. They were allowed to acclimatize for seven days prior to the start of the treatment. The weights were determined and were separated into five groups of six rats each. Groups A, B, C, D served as the experimental groups, while group E served as the control. Animals in group A were exposed to 130 mg/kg body weight (10% of LD_{50}) of *X. aethiopica* fruit extract, those in group B were treated with 259 mg/kg body weight (20% of LD_{50}) of *X. aethiopica* fruit extract, those in group C were exposed to 389 mg/kg body weight (30% of LD_{50}) of *X. aethiopica* fruit extract, those in group D were treated with 518 mg/kg body weight (40% of LD_{50}) of *X. aethiopica* fruit extract, while those in group E (control) received normal animals feeds

and water only. The treatment was done once daily for 28 days via oral route. After 28 days treatment, the animals were sacrificed under ether anaesthesia in a desiccator after an overnight fast. Blood was taken from the rats through cardiac puncture.

2.5 Determination of Female Reproductive Hormones

Serum levels of follicle stimulating hormone (FSH), luteinizing hormone (LH), progesterone, estrogen and prolactin were determined using enzyme-linked immunosorbent assay (ELISA) technique described by Tanv and Harkaran [20].

2.6 Statistical Analysis

Data were analyzed using Graph Pad Prism software. Results were expressed as Mean \pm Standard Deviation (SD). A one-way analysis of variance (ANOVA) was used to compare the mean, followed by Tukey's post hoc test. Differences between means were considered to be significant at $p \leq 0.05$.

3. RESULTS

3.1 Median Lethal Dose (LD_{50}) Result

The visible signs of toxicity of *X. aethiopica* fruit extract observed in this study are excitation, decreased motor activity, paw licking, increased respiratory rate, gasping and coma which could be followed up by death. In the first phase of the median lethal dose determination, no death was observed in the group administered 1000 mg/kg body weight of *X. aethiopica* fruit extract. However, all the animals died in the groups exposed to 2000, 3000, 4000, and 5000 mg/kg body weight of *X. aethiopica* fruit extract respectively (Table 1). In the same vein, in the second phase of medial lethal dose determination, no death was recorded in the group treated with 1200 mg/kg body weight of *X. aethiopica* fruit extract while 100% mortality was recorded in the groups treated with 1400, 1600, and 1800 mg/kg body weight of *X. aethiopica* fruit extract respectively as presented in Table 1.

The median lethal dose (LD_{50}) was computed as geometrical average of the maximum dose yielding 0% death (a) and the minimum dose yielding 100% death (b).

$$LD_{50} = \sqrt{ab}$$

Where a = 1200 mg/kg

b = 1400 mg/kg

LD₅₀= 1296.15 mg/kg

3.2 Effect of ethanol extract of *Xylopi* *aethi* *opica* fruit on Female Reproductive Hormones of Animals after 28 days of Treatment

A non-significant increase was observed in the blood concentration of FSH when animals treated with 130 mg/kg body weight (low dose) of *Xylopi* *aethi* *opica* extract were compared with those in the control group (P = 0.05), as presented in Table 2. Increase in the dose of *Xylopi* *aethi* *opica* extract resulted in a decrease in serum FSH levels. This decrease was significant when the FSH levels of animals treated with 389 mg/kg and 518 mg/kg body weight of ethanol extract of *Xylopi* *aethi* *opica* fruit were respectively compared with those in the control group (P<0.05). Administration of ethanol extract of *Xylopi* *aethi* *opica* fruit to animals for 28 days led to a dose-dependent decrease in the serum level of luteinizing hormone (LH). This decrease was only significant (P = 0.01) when the LH levels of

animals treated with 259, 389 and 518 mg/kg of *Xylopi* *aethi* *opica* extract were respectively compared with those in the control group. The result of this study indicates that extract of *Xylopi* *aethi* *opica* decreased serum level of progesterone in female rats at low doses of 130 mg/kg and 259 mg/kg. The decrease was only significant (P<0.05) at the lowest dose of 130 mg/kg when compared with those in the control group. However, increase in the dose of the extract increases the serum progesterone concentrations. The increase became significant (P = 0.02) when the concentration of serum progesterone in animals treated with 518 mg/kg of *Xylopi* *aethi* *opica* extract were compared with those in the control group. Administration of *Xylopi* *aethi* *opica* extract to animals for 28 days led to a dose-dependent decrease in the serum level of estrogen. This decrease was only significant (P<0.05) when the estrogen levels of animals treated with 389 mg/kg and 518 mg/kg of *Xylopi* *aethi* *opica* extract were respectively compared with those in the control group. Conversely, *Xylopi* *aethi* *opica* extract increases serum levels of prolactin in a dose-dependent manner. The increase was however nonsignificant (P<0.05) when the prolactin levels of animals treated with 130 mg/kg (low dose) of *Xylopi* *aethi* *opica* extract were compared with those in the control group.

Table 1. The Median lethal dose (LD₅₀) of *Xylopi* *aethi* *opica* fruit extract

Study (Animal)	Phase/ Dosage of Extract (mg/kg) b.w	No of Mice per Group	No. of Death Recorded	% Mortality
PHASE ONE				
I	1000	5	0	0
II	2000	5	5	100
III	3000	5	5	100
IV	4000	5	5	100
V	5000	5	5	100
PHASE TWO				
I	1200	5	0	0
II	1400	5	5	100
III	1600	5	5	100
IV	1800	5	5	100
V	2000	5	5	100

LD₅₀= 1296.15 mg/kg

Table 2. Effect of ethanol extract of *Xylopi* *aethi* *opica* fruit on Female Reproductive Hormones of Animals after 28 days of Treatment

Group	A	B	C	D	E	P Value
Dose of extract (mg/kg)	130	259	389	518	Control	
FSH (mg/dL)	20.52±2.15	16.84±3.08	11.47±2.26*	9.33±1.42*	18.77±2.26	0.05
LH (mg/dL)	31.89±7.08	29.03±3.82*	24.41±3.33*	20.72±3.06*	34.98±5.07	0.01
Pg (ng/dL)	11.03±2.62*	16.67±3.27	23.55±2.99	28.22±4.01*	19.71±2.13	0.02
Estrogen (mg/dL)	29.11±3.38	26.45±4.10	24.06±2.44*	20.98±3.04*	33.02±7.25	0.04
Prolactin (ng/dL)	25.09±2.35	30.27±4.05*	32.33±3.62*	38.02±3.84*	20.14±4.04	0.05

Values are presented as Mean±S.D, where n = 6. Values with * are statistically significant at p value ≤ 0.05 when compared with the control group.

Legend: FSH = Follicle Stimulating Hormone, LH = Luteinizing Hormone, Pg = Progesterone

4. DISCUSSION

The acute toxicity study of the plant extracts recorded 100% mortality at a dose of 1400 mg/kg bodyweight and above (Table 1). This shows that the fruit of *Xylopi aethiopica* might be highly toxic. The visible signs of toxicity seen in the animals are excitation, paw licking, increased respiratory rate, decreased motor activity, gasping and coma which was followed by death.

The results of the impact of ethanolic fruit extract of *Xylopi aethiopica* on female reproductive hormones of Wistar rats after twenty-eight days of exposure are shown in table 2. The ability of pre-ovulatory follicles to mature as well as for ovulation to occur is controlled by the effects of ovarian and extra ovarian hormones. Perturbations in the levels of these hormones result in irregularity in the functions of the ovarian as well as the period of estrous cycle [21]. These perturbations in hormones could be a reflection of several components of plants [22]. Maintaining homeostasis in human reproductive hormones is vital [23]. To achieve a success in fertility during the first half of the menstrual cycle, concentrations of estrogen increase and influence the growth and elevation of uterine cells. Sequel to the FSH, an ovum starts developing within one of the ovaries. On the 14th day of a 28-day cycle, an ovary is released in response to the LH, and a rise in the concentration of progesterone happened during the second half of the menstrual cycle, which leads to an elevation in the thickness of the lower limb [24]. In this present study, a nonsignificant elevation was seen in the blood

concentration of follicle stimulating hormone (FSH) when animals exposed to 130 mg/kg body weight (low dose) of ethanol extract of *Xylopi aethiopica* fruit were compared with those in the control group. Increase in the dose of *Xylopi aethiopica* extract resulted in decrease in serum FSH levels. This decrease was significant (P<0.05) when the FSH levels of animals exposed to 389 mg/kg and 518 mg/kg body weight of *Xylopi aethiopica* extracts were respectively compared with those in the control group. FSH is the main reproductive hormone in mammals, useful in the development of the gonad and maturation at puberty and the production of gamete in the fertile phase of life [25]. It enhances the growth and maturation of ovarian follicles by acting directly on the receptors located on the granulose cells [22]. The decline in the FSH concentration by fruit extract of *Xylopi aethiopica* at high doses might hinder folliculogenesis and prolong maturation of the follicle in the pre-ovulatory phase [26]. The reduction in the blood concentration of FSH at these doses is similar to the study of Nnodim *et al.* [27] who observed a decrease in serum FSH when animals were treated with high doses of *Xylopi aethiopica* fruit extract. It could also mean that the extract at the administered doses could have exhibited its potential on the anterior pituitary or the hypothalamus since the secretion of stimulating hormone is regulated by the gonadotropic releasing hormone secreted by the hypothalamus [28]. The decline seen in the concentration of this hormone could have a negative effect on conception in female animals and possibly humans. The major role of FSH is to induce gametogenesis and follicular

development in females [29]. In females, FSH facilitates the maturation of follicular cells of the ovary. Steroidogenic functions in females are dependent on other hormonal factors such as LH while FSH induces the conversion of androgens to estrogens [30]. The decrease in circulating FSH observed in this study could also be attributed to the overall effect of metabolism. Since steroids reduce FSH synthesis and extracts of *Xylopiya aethiopic*a fruit contains steroids [7], it might be suggestive that steroids could also possibly be responsible for decrease in circulating FSH level observed in this study.

Luteinizing hormone (LH) is known to induce the release of reproductive steroids from the gonads [31]. In females, ovulation of mature follicles in the ovary is stimulated by a surge of luteinizing hormone secretion during the pre-ovulatory periods. Several authors have demonstrated that LH release surges at the pre-estrous stage were responsible for ovulation [22, 26]. Any substance with the ability of inhibiting this secretion could provoke disruption of ovulation by reducing the number of mature follicles or induce an estrous cycle disruption at rest [32,33]. The significant decline seen in the concentration of serum LH in this study (especially at high doses) might indicate an inhibitory effect of the extract on the release of LH which may trigger the disruption of ovulation. This might result in impairment of estrous cycle, hamper conception and normal reproduction in females. It is therefore possible that *X. aethiopic*a fruit contains anti-gonadotropic substance which might affect the estrous cycle and hamper reproduction in females [34].The reduction in the serum level of LH observed in this study is dose-dependent.

Progesterone which is produced in the ovaries, placenta, and adrenal glands, helps to regulate the monthly menstrual cycle, prepare the body for conception and pregnancy as well as stimulate sexual desire [35]. The hormone also encourages the growth of milk-producing glands in the breast during pregnancy. High progesterone levels were believed to be partly responsible for symptoms of premenstrual syndrome (PMS), such as breast tenderness, feelings of bloat and mood swings. The feedback inhibition of Gonadotropin-releasing hormone (GnRH) secretion by estrogens and progesterone provides the basis for the most widely-used form of contraception. Such feedback inhibition of GnRH prevented the mid

cycle surge of LH and ovulation [36]. The result of this study indicates that extract of *X. aethiopic*a decreased serum level of progesterone in female rats at low doses of 130 mg/kg and 259 mg/kg. The decrease was more significant ($P<0.05$) at the lowest dose of 130 mg/kg when compared with those in the control group. The reduction in the levels of serum progesterone by *Xylopiya aethiopic*a extract at these doses might produce consequential effect on conception in females; impede ovulation which might result in annovulation and sequelae [22]. Alkaloids had equally been reported to inhibit the synthesis of cellular progesterone [37]. Therefore, the reduced level of progesterone by *Xylopiya aethiopic*a may not be unconnected with the alkaloidal component of the extract. This result is consistent with the findings of Onuka *et al.*, [38] who reported an increase in the level of progesterone when animals were treated with low doses of *Xylopiya aethiopic*a fruit extracts. However, increase in the dose (388.5 and 518 mg/kg) of the extract in this study increased the serum progesterone concentrations. The increase became significant ($P<0.05$) when the concentration of serum progesterone in animals treated with 518 mg/kg of *Xylopiya aethiopic*a extract were compared with those in the control group. The phytochemical evaluation of *Xylopiya aethiopic*a fruit revealed that it contains alkaloids, saponin, tanins, Coumarin, phlobatannins, anthraquinones, steroids, flavonoids, cardiac glycosides and so on [7]. Yun *et al.*, [39] cited in Egba *et al.*, [26] had reported that high dose of extract of *Xylopiya aethiopic*a, containing saponins lowered serum androgens and 17β -estradiol, but elevated progesterone levels, suggesting that saponins might modulate steroidogenesis in the ovary. High level of progesterone has antiestrogenic effect on the myometrial cell, decreasing their excitability, their sensitivity to oxytocin, and their spontaneous electrical activity while increasing their membrane potential [40]. The increase observed in the serum concentration of progesterone in this study sequel to administration of high dose of *Xylopiya aethiopic*a fruit extract was in line with the findings of Nnodim *et al.*, [27] who investigated the effects of *Xylopiya aethiopic*a fruits on reproductive hormonal level in rats. Decrease in serum levels of FSH and LH had been reported to increase progesterone concentration in Wistar rats [41]. Therefore, the increase observed in the concentration of progesterone in this study

following the administration of high dose of *Xylopiya aethiopic*a might be due to the reduction in the concentrations of FSH and LH observed in this study. Increase in serum progesterone concentrations had been speculated to indirectly predispose animals to teratogenicity and carcinogenesis [42]. Thus, the increase observed in the serum level of progesterone in this study at high doses suggested that extracts of *Xylopiya aethiopic*a might indirectly predispose its consumers to teratogenicity and carcinogenesis when consumed in high dosage.

Estrogen stimulates the growth of the uterine lining, causing it to thicken during the pre-ovulatory phase of the cycle. It is well established that estrogen is directly responsible for growth and development of reproductive organs. In synergy with follicle stimulating hormone, estrogen stimulates granulosa cell proliferation during follicular development. Plants with estrogenic properties can directly influence pituitary action by peripheral modulation of luteinizing hormone and follicle stimulating hormone, decreasing secretion of these hormones and blocking ovulation. Thus, the reduction in the serum concentration of estrogen observed in this study might be attributed to a decreased aromatase activity or substrate supplementation during estrogen synthesis [43]. Consequently, such decrease in estrogen levels may hamper ovulation, preparation of the reproductive tract for zygote implantation and the subsequent maintenance of pregnancy state [43]. Kadohama *et al.*, [44] had reported that several plant alkaloids inhibit aromatase activity. Thus, it is possible that the phytochemical content of extract of *Xylopiya aethiopic*a may disrupt endocrine activity and possibly induce hormonal imbalance or disorders such as anti-fertility and contraception in hormone dependent organs like the ovary and mammary glands. The findings in this study have important implications for female contraceptive development. The reduction in the serum level of estrogen observed in this study is consistent with the report of Adienbo *et al.*, [45] who observed a dose dependent decrease in the number of pregnant females in all the test groups when they studied the contraceptive efficacy of hydro-methanolic fruit extract of *Xylopiya aethiopic*a in male albino rats.

In the context of this study, ovaries are central in the synthesis of estrogen and could be altered by the extract. During the process of

folliculogenesis, thecal and granulosa cells are involved in the estrogen synthesis. Theca cells can not directly produce estrogen and therefore in growing follicles, androgens are released from the thecal cells and transported to the granulosa cells where P₄₅₀ aromatase enzyme converts androgens to estrone and 17-beta estradiol [46]. In addition to saponin, flavonoids are one of the major phytochemical contents of the *Xylopiya aethiopic*a fruit extract. Studies have shown that saponins and flavonoids inhibit aromatase enzyme in human preadipocyte [47] and inhibition of aromatase enzyme has been shown to reduce estrogen production throughout the body to nearly undetectable levels [48]. To a large extent, estrogen from androgen conversion contributes to the estrogen pool. Moreover androgen production from the thecal cells is largely under the control of LH from the pituitary [49]. Therefore, the decrease in LH observed in this study could impair androgen production and inhibit the conversion of androgens into estrogens in the granulosa cells resulting in the reduction of estrogen level. This result is consistent with the findings of Onuka *et al.*, [38] who reported a decrease in estrogen concentration sequel to *Xylopiya aethiopic*a administration. FSH has also been reported to stimulate the conversion of androgens to estrogens [30]. The decrease in the level of estrogen might also be attributed to the observed decrease in the concentration of serum FSH in this study. Estrogen production by the ovary or corpus luteum occurs as a result of interplay of different endocrine glands and enzymes [50]. It is possible that *Xylopiya aethiopic*a fruit was able to reduce estrogen concentration by interfering with one of the steps or enzymes that lead to its production.

The enhanced level of prolactin observed in this study might be attributed to the effect of the extract probably acting as a dopamine antagonist. The elevated level of prolactin in this study justifies the folklore use of the plant in stimulating lactation. The result of this study is consistent with the findings of Onyebuagu *et al.*, [34], Anacletus *et al.*, [51] and Ehigiator and Adikwu [52] who respectively reported an increase in serum prolactin level when they administered different doses of *Xylopiya aethiopic*a extracts on female Wistar rats. The increase serum prolactin was as a result of increased synthesis and secretion of prolactin in the anterior pituitary in response to hormonal factors such as thyrotropin-releasing hormone

and oxytocin, physiological signals such as sleep, stress, pregnancy and tactile signals during weaning, whereas, reduction in the circulating prolactin can be traced to the activity of prolactin-inhibiting hormone, dopamine and tissue-specific prolactin clearance by ovary, liver, kidney and mammary gland during lactation [53]. The concentration of prolactin in the serum at any time is therefore influenced by the factors inducing synthesis, those inhibiting synthesis and turnover rate at the target cells [54]. These hormonal imbalances observed in this study might be caused by numerous chemical agents contained in the extract. Yakubu *et al.* [22] and Benie *et al.* [32] independently reported that phytochemical screening has revealed many bioactive as well as toxic agents of plant extract that could affect the regulation of estrous cycle, conception and reproduction. Alkaloids and flavonoids have been shown to reduce plasma concentrations of estrogen [54]. Therefore, the presence of these phytochemicals in *Xylopi a aethiopi ca* fruit may account for the alterations in the levels of the circulating hormones observed in this study. Our previous study [18] showed that extracts of *Xylopi a aethiopi ca* fruit reduced sperm qualities in Wistar rats and might result in infertility in male rats. This is suggestive that the fruit has the propensity to induce infertility in both male and female rats.

5. Conclusion

The effect of *Xylopi a aethiopi ca* extract on female reproductive hormones observed in this study showed that the extract might be a potent contraceptive. Plant products as contraceptive will be more acceptable for economic reasons and for the fact that they are associated with minimum side effects than synthetic agents.

CONSENT

It is not applicable.

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Comment [AaM3]: Please add a recommendation for further studies investigating the contraceptive effect of this extract in mating animals.

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