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Original Research Article

Effect of *Xylopia aethiopica* Fruit on the Histopathology of Selected Organs from Treated Wistar Rats

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Abstract

Traditionally, the use of *Xylopia aethiopica* fruit for therapeutic purposes is on the increase without any consideration of its safety and toxicity. This study was therefore aimed at investigating its effect on the histopathology of selected organs from Wistar rats. The fruits of *Xylopia aethiopica* were air-dried and extracted by Soxhlet extractor using ethanol as a solvent. Thirty wistar rats of both sexes were divided into five groups of six rats each. Animals in groups 1, 2, 3, and 4 were treated with 130, 259, 389 and 518 mg/kg body weight of *X. aethiopica* 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. At the end of the treatment, animals were sacrificed under ether anaesthesia in a desiccator after an overnight fast. Organs (liver, kidney, stomach, heart, testis, uterus, and ovary) were harvested and preserved using 10% formal saline solution for further analysis. Histological examination was later performed on them. The extract was observed to induce damage on the selected organs especially at high doses thereby authenticating its perceived toxicity.

Keywords: Contraceptive, Histological Examination, Organ Damage, Toxicity, *Xylopia aethiopica* Fruit

INTRODUCTION

Xylopia aethiopica 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 (Burkill, 2004). A preparation of the stem bark or fruit is helpful in the management of bronchitis, stomach aches, asthma, and dysenteric conditions. The seed extract is helpful as a vermifuge for roundworms (Dalziel, 2005). Several postnatal women take 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 (Ezekwesili *et al*., 2010). Medicinal plant extracts with a therapeutic property has the tendency of wrong prescription and sometimes, overdosed. The fact that *Xylopia aethiopica* is a natural product does not automatically confers on it safety and might be risky to its consumers. Chemical ingredients of the plant are perceived to be useful in preventing and managing cancerous tumors (Del-Rio *et al*., 1997). *Xylopia aethiopica* fruit is known to have alkaloids, terpenoids, flavonoids, and organic oils (Iwu, 1993; Shanmugam *et al*., 2008). Figure 1

Figure 1. *Xylopia aethiopica* Fruit (Ogbuagu *et al*., 2020a)

Xylopia aethiopica is characterized with numerous chemical components with various medicinal potentials (Nwafor *et al*., 2009). 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 (Esekhiagbe *et al*., 2009; John-Dewole *et al*., 2012), alkaloids, rutin and fixed oils (Asekun and Kunle, 2004; Nwaichi and Igbinobaro, 2012). The plant has also be 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 (John-Dewole*et al*., 2012; Nwaichi and Igbinobaro, 2012). The impact of the fruit on body weight and glucose concentration of animals has been reported (Ogbuagu *et al*., 2020b). Ogbuagu *et al*., (2020c) has also reported its effect on lipid profile of animals. Other studies have reported its hepatotoxicity (Ogbuagu *et al*., 2021a), renal toxicity (Ogbuagu *et al*., 2021b) as well as oxidative stress (Ogbuagu *et al*., 2022a). Recently, Ogbuagu *et al*. (2022b), reported that the fruit extract of *Xylopia aethiopica* adversely perturbed sperm qualities in male Wistar rats. With these reported toxicity, this study was designed to investigate if its effect on the histopathology of Wistar rats correlates with the previous toxicity reports.

MATERIALS AND METHODS

Collection and Authentication of Plant Materials

The fruits of *Xylopia aethiopica* were sourced from a market in Aba, Abia State. They were identified and authenticated by Prof. Margaret Bassey of Botany and Ecological Studies Department, University of Uyo. It was assigned a voucher number of UU/PH/4e and deposited in the Herbarium of the Department of Pharmacognosy and Natural Medicine, University of Uyo, Akwa-Ibom State, Nigeria.

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*. (2020a). 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.

Experimental Design

Thirty Wistar rats of both sex 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 1, 2, 3, 4 served as the experimental groups, while group 5 served as the control. Animals in group 1 were exposed to 130 mg/kg body weight (10% of LD_{50}) of *X. aethiopica* fruit extract, those in group 2 were treated with 259 mg/kg body weight (20% of LD_{50}) of *X. aethiopica* fruit extract, those in group 3 were exposed to 389 mg/kg body weight (30% of LD_{50}) of *X. aethiopica* fruit extract, those in group 4 were treated with 518 mg/kg body weight (40% of LD_{50}) of *X. aethiopica* fruit extract, while those in group 5 (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. Organs were harvested and preserved using 10% formal saline solution for further analysis.

Histopathological Analysis of Animals' Organs

The histopathological examination of animals' organswas done according to the method of Humphrey and kumaratilake, (2017). Briefly, the organs were cut into sizes of about 0.5 cm thick on a slab and fixed in Bouin's fluid for about 24 hours and transferred to ascending alcohol concentration for dehydration. Each piece was directly put into 70% alcohol for six hours and then to 90% alcohol overnight. It was then transferred to 3 changes of absolute alcohol for one hour each, and later put into chloroform for 10 hours and fresh chloroform for about 30 minutes. The tissues were placed vertically in molten paraffin wax inside a metal mould and left overnight to cool and solidify. They were later trimmed and mounted on wooden blocks. Serial sections of 6 microns thick were obtained using a rotatory microtome. The deparaffinize sections were stained routinely with haematoxylin and eosin. Photomicrographs of desired sections were made.

RESULTS AND DISCUSSION

The results of the histopathological investigation of the liver of animals treated with high doses (389 and 518) mg/kg of ethanol extract of *Xylopia aethiopica* fruit showed the central vein area with infiltrating inflammatory cells, vacuolated hepatocytes, wide area of degenerating hepatic cells, widely spread macrovessicular steatosis and irregular orientation in the sinusoidal arrays of the liver tissue. The degeneration of the hepatic tissue by *Xylopia aethiopica* administration in this study correlated with the elevation of hepatic biomarkers reported by Ogbuagu *et al*. (2021a) when they exposed animals to *Xylopia aethiopica* fruit for 28 days. This showed that the integrity of the liver had been compromised sequel to *Xylopia aethiopica* fruit administration (Shittu *et al*., 2015). Thus, *Xylopia aethiopica* fruit is hepatotoxic especially at high doses (above 389 mg/kg). The finding agreed with the report by Obodo *et al*. (2013) that the administration of *Xylopia aethiopica* could induce hepatic cell damage resulting from the elevation of liver enzymes because of the presence of xylopic acid in its constituent.

Observations from the histopathological study of the kidney treated with 389 and 518 mg/kg of ethanol extract of *Xylopia aethiopica* fruit showed a nephrotic cortical area with degenerating glomeruli, widened and occluding Bowman spaces, degenerating ductal cells, connective tissue degeneration and hemorrhagic blood tissue within the renal tissue. These degenerations of the renal tissues are consistent with the significant elevation of renal biomarkers observed by Ogbuagu*et al*. (2021b) when they administered ethanol extract of *Xylopiaaethiopica* fruit to animals for 28 days. This suggests that treatment of animals with *Xylopia aethiopica* fruit compromised the integrity of the kidney and therefore possesses a nephrotoxic effect. This corresponded to the findings ofYusuf*et al.* (2018) who reported the hepato- and nephrotoxicity of Nigerian *Xylopia aethiopica* seed extract.

The histopathology of the stomach of animals treated with 389 and 518 mg/kg of ethanol extract of *Xylopia aethiopica* fruit showed a gastric mucosa with disoriented gastric pits, degenerating gastric cells, wide areas of hyperplastic gastric cells and the gastric gland. This suggests that *Xylopia aethiopica* fruit is toxic to the stomach and possesses the propensity to induce or aggravate gastric ulceration. This contradicted the work carried out by Agbai*et al.,* (2017), who demonstrated that oral administration of *Xylopiaaethiopica* seed extract resulted in a significant reduction in free acidity and gastric volume.

The photomicrograph of the longitudinal section of the right ventricular tissue of the heart treated with 518 mg/kg (40% of LD_{50}) of ethanol extract of *Xylopia aethiopica* fruit showed the cardiac tissue with numerous cardiac myocyte nuclei, vacuolated cardiac myocyte, presence of macrophagic cells and disorientations of the cardiac muscle fibres. With these toxic effects on heart tissues, continuous consumption of *Xylopia aethiopica* fruit especially at high doses might lead to myocardial infarction and other cardiovascular diseases. The effect of*Xylopia aethiopica* fruit on lipid profile has been reported (Ogbuagu *et al*., 2020c).

The results of the histopathological investigation of the testis of animals treated with ethanol extract of *Xylopia aethiopica* fruit showed a dose-dependent degeneration of spermatogenic cells and widening of tubular lumen. This is suggestive that the extract is toxic to the testis.

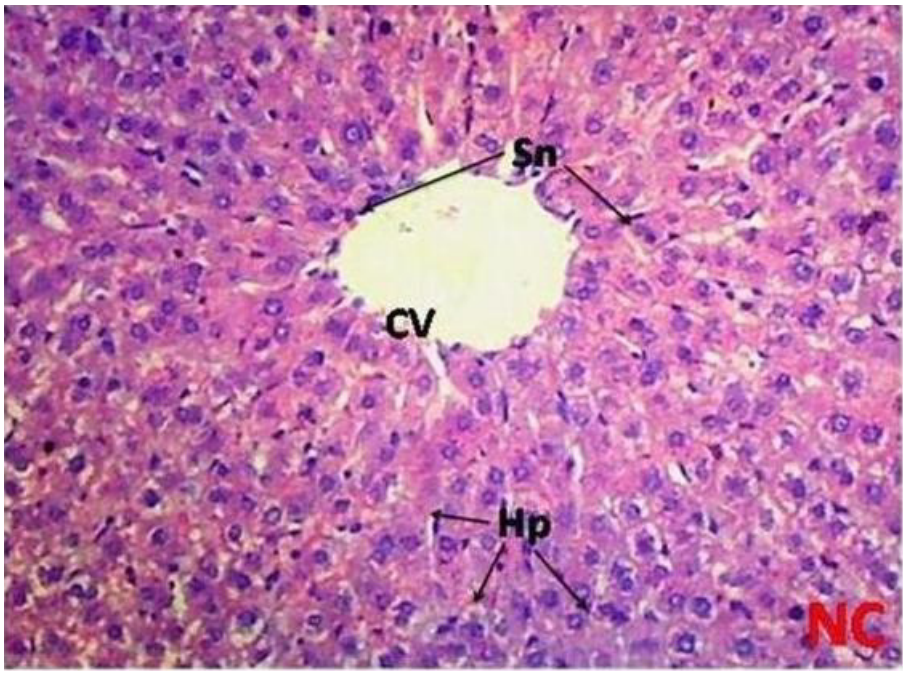

Plate 1. Photomicrograph of Normal Control (NC) group reveals normal histoarchitecture of the liver with numerous hepatocytes, well oriented arrays of sinusoids, and a central vein with organized vascular epithelial layer. Mag x100 (H& E)

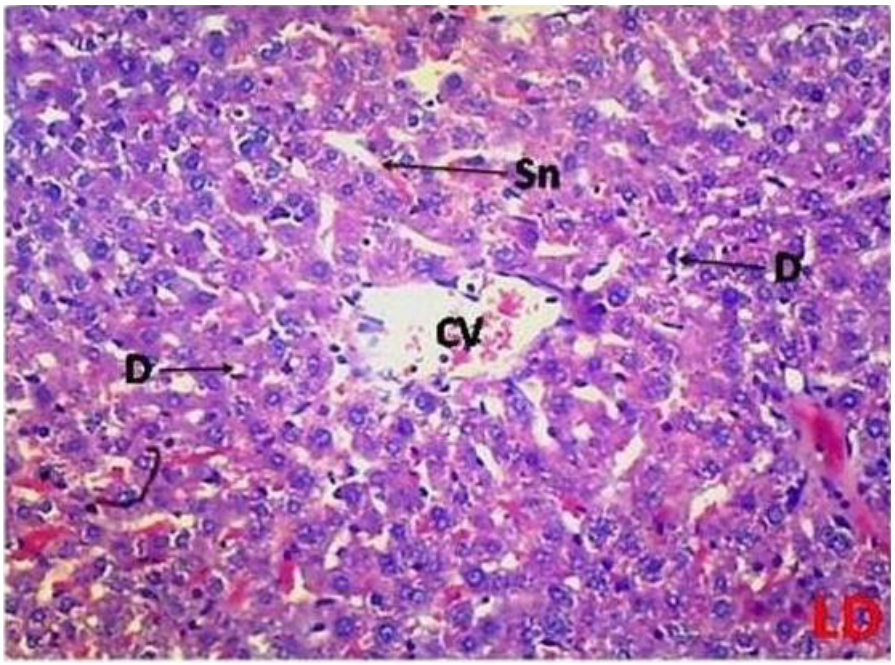

Plate 2. Photomicrograph of the section of the liver tissue of the low dose (LD) animals treated with130 mg/kg (10% of LD50) of ethanol extract of *Xylopiaaethiopica* fruit showing the central vein (CV) with mild vascular epithelial distortion, degenerating hepatocytes (D), and irregular orientation of the arrays of sinusoids. Mag.x100 (H&E)

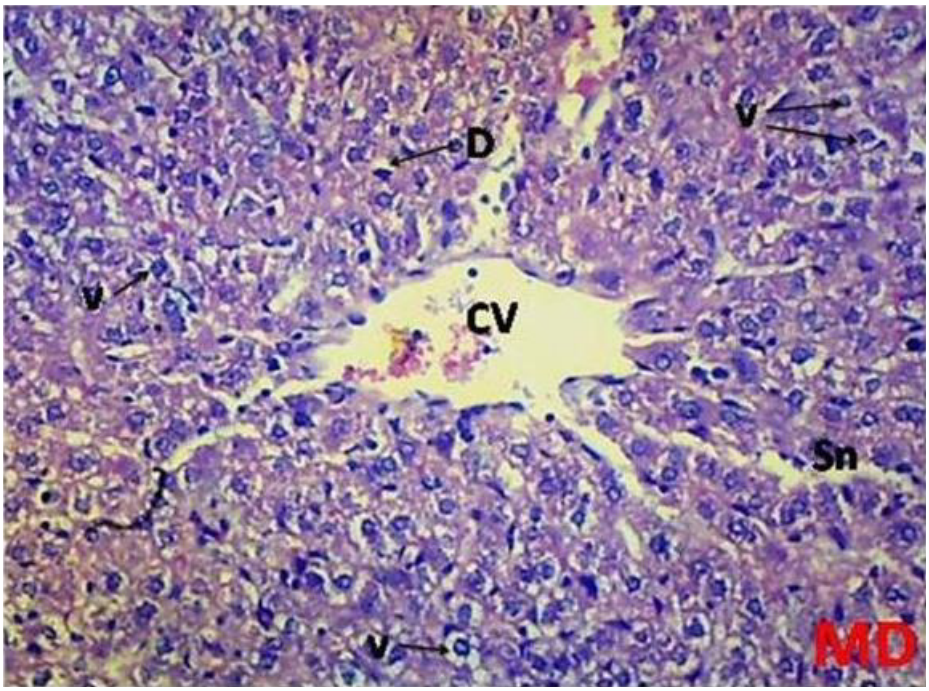

Plate 3. Photomicrograph of the section of the liver tissue of the medium dose (MD) animal treated with 259mg/kg (20% of LD50) of ethanol extract of *Xylopia aethiopica* fruit showing the central (CV) area with altered vascular epithelium, degenerated hepatocytes (D), wide area of vacuolated hepatocytes (v) and abnormal orientation of arrays of sinusoids. Mag.x100 (H&E).

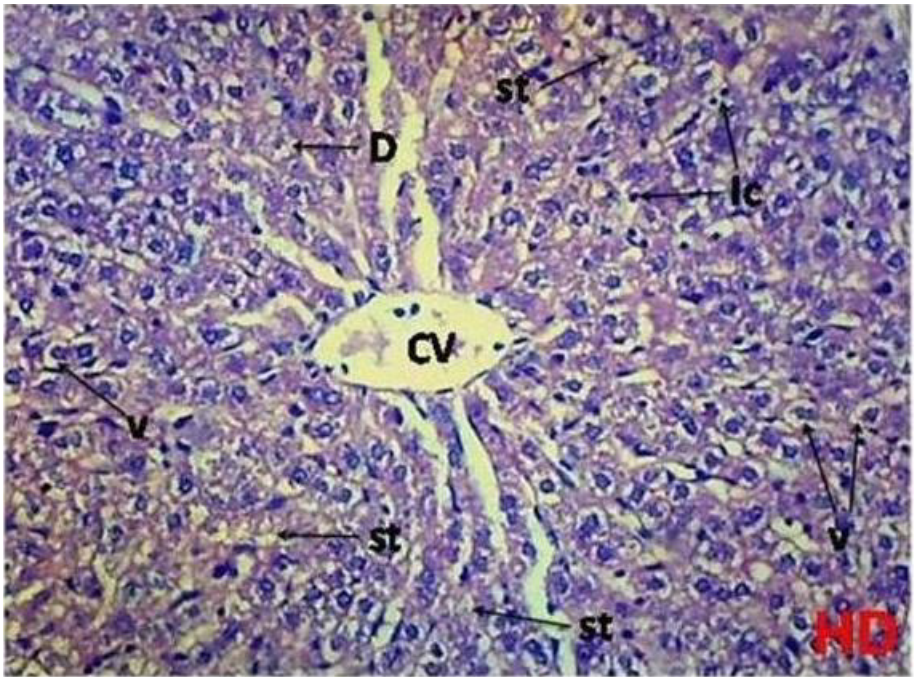

Plate 4. Photomicrograph of the section of the liver tissue of the High dose (HD) animal treated with 389 mg/kg (30% of LD_{50}) of ethanol extract of *Xylopia aethiopica* fruit showing the central vein with vacoulated hepatocytes (v), wide distribution of microvessicular steatosis (st), degenerations of the hepatic cells (D). Mag. x100(H&E).

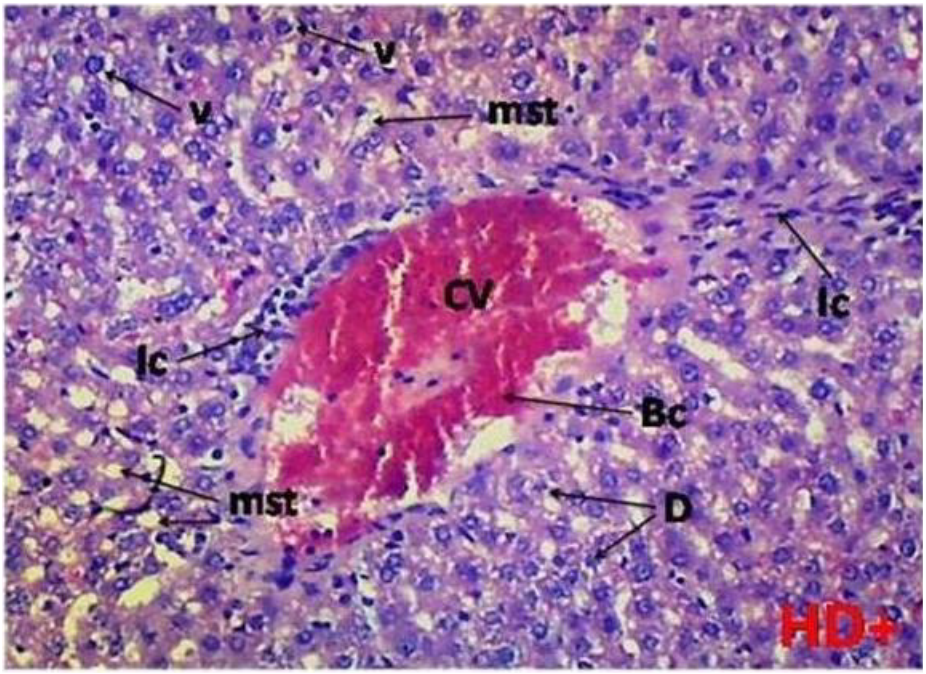

Plate 5. Photomicrograph of the section of the liver tissue of the higher dose (HD+) animal treated with 518 mg/kg (40% of LD_{50}) of ethanol extract of *Xylopia aethiopica* fruit showing the central vein area with infiltrating inflammatory cells (IC), vacuolated hepatocytes (v), wide area of degenerating hepatic cells (D) widely spread macrovessicular steatosis (mst) and irregular orientation in the sinusoidal arrays. Mag.x100(H&E).

Effect of Ethanol Extract of *Xylopia aethiopica* Fruit on the Kidney of an Adult Wistar Rat

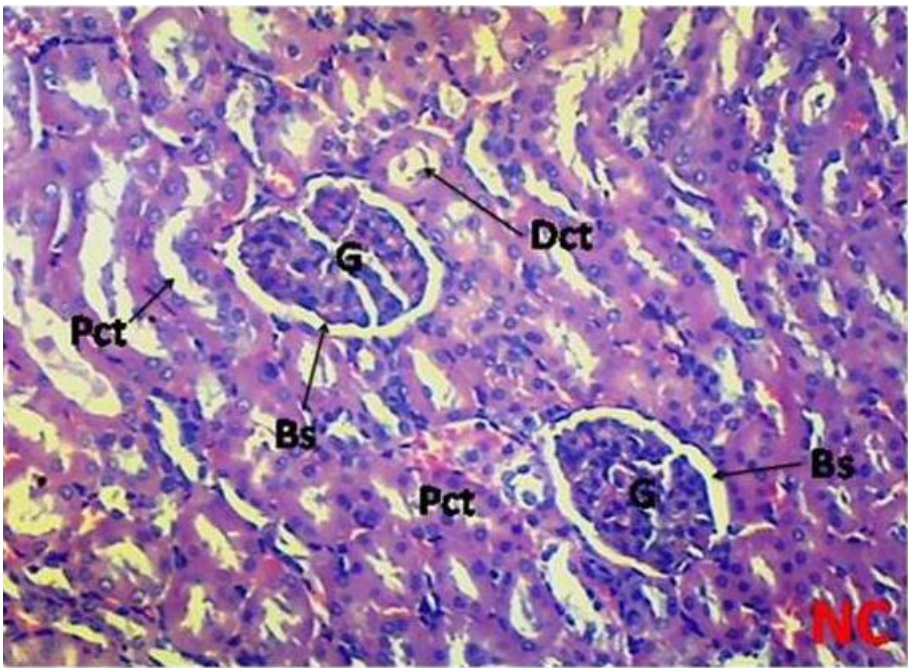

Plate 6. Photomicrograph of the transverse section of the kidney of the normal control (NC) group showing the necrotic cortical area with well-presented glomeruli (G), proximal convoluted tubules (Pct), Distal convoluted tubules (Dct) and normal bowman's spaces (Bs) within the renal tissue. Mag.x100(H&E).

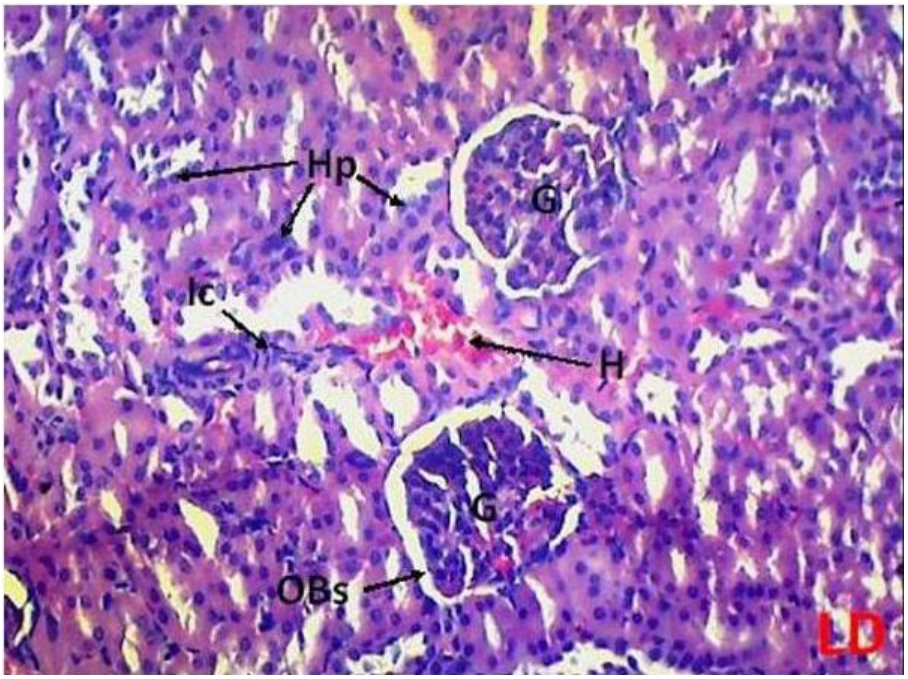

Plate 7. Photomicrograph of the transverse section of the kidney of the Low dose (LD) animal treated with 130mg/kg (10% of LD_{50}) of ethanol extract of *Xylopiaaethiopica* fruit showing the nephrotic cortical area with glomerulli and gradual occluding bowman's space (Obs) blood vessel with surrounding inflammatory cells (IC), areas of hyperplastic ductal cells and hemorrhagic blood tissue (H) within the renal tissue. Mag,x100(H&E).

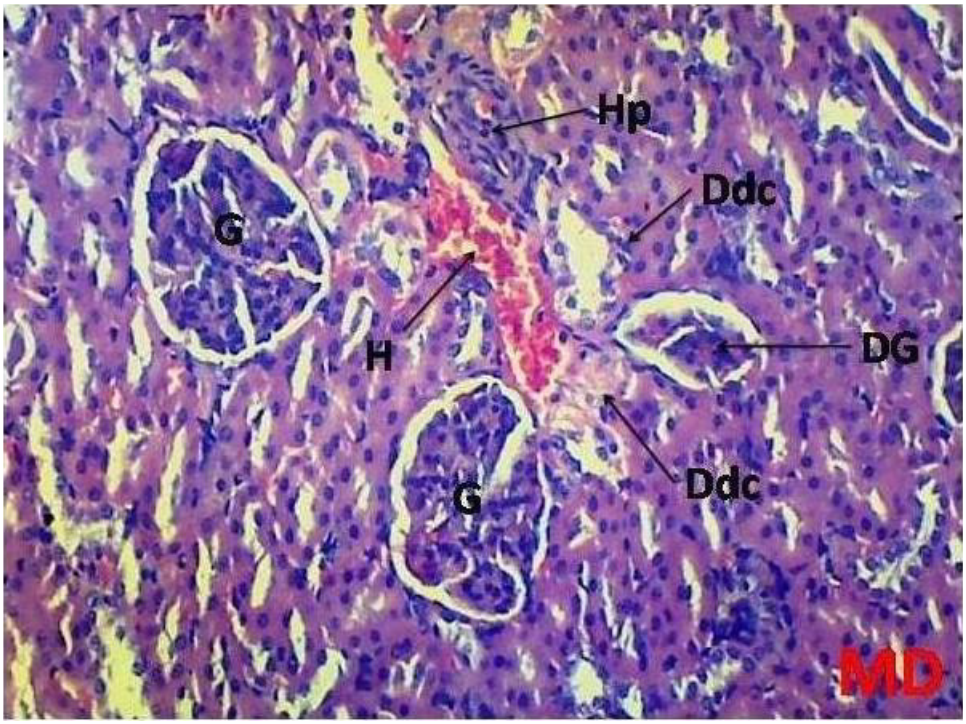

Plate 8. Photomicrograph of the transverse section of the kidney of the medium dose (MD) animal treated with 259 mg/kg (20% of LD_{50}) of ethanol extract of *Xylopia aethiopica* fruit showing the nephrotic cortical area with degenerating glomerulus (DG), degenerating ductal cells (Ddc), hyperplastic vascular cells (HP), and hemorrhagic blood tissue (H) within the renal tissue. Mag.x100(H&E).

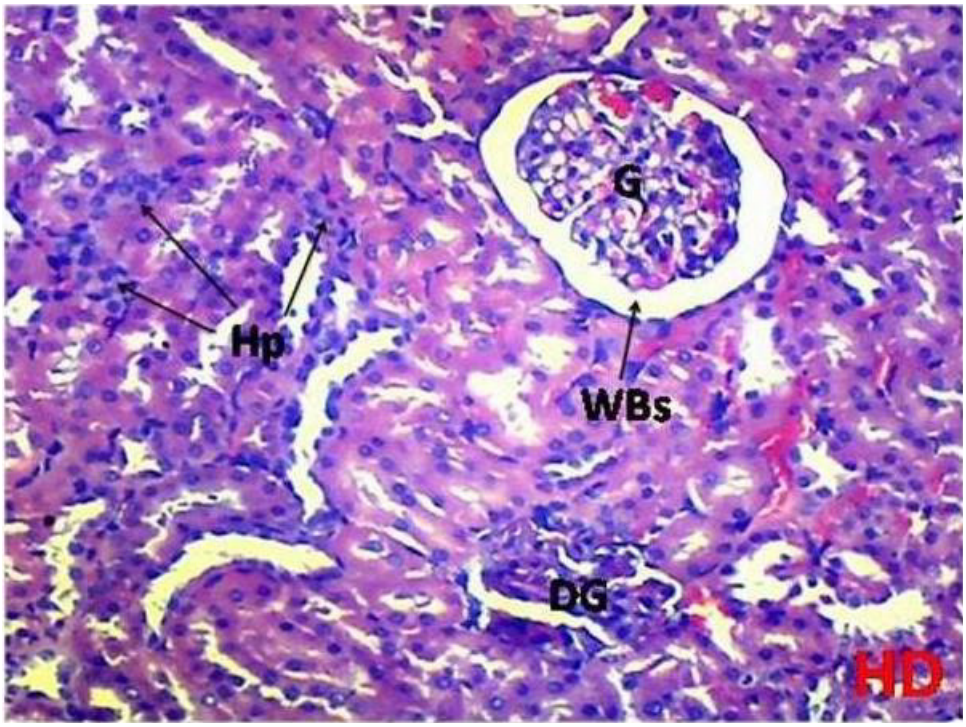

Plate 9. Photomicrograph of the transverse section of the kidney of the High dose (HD) animal treated with 389mg/kg (30% of LD50) of ethanol extract of *Xylopia aethiopica* fruit showing the nephrotic cortical area with degenerating glomeruli (DG), widened bowman's space (WBs) and wide area of hyperplalstic ductal cells within the renal tissue. Mag.x100(H&E).

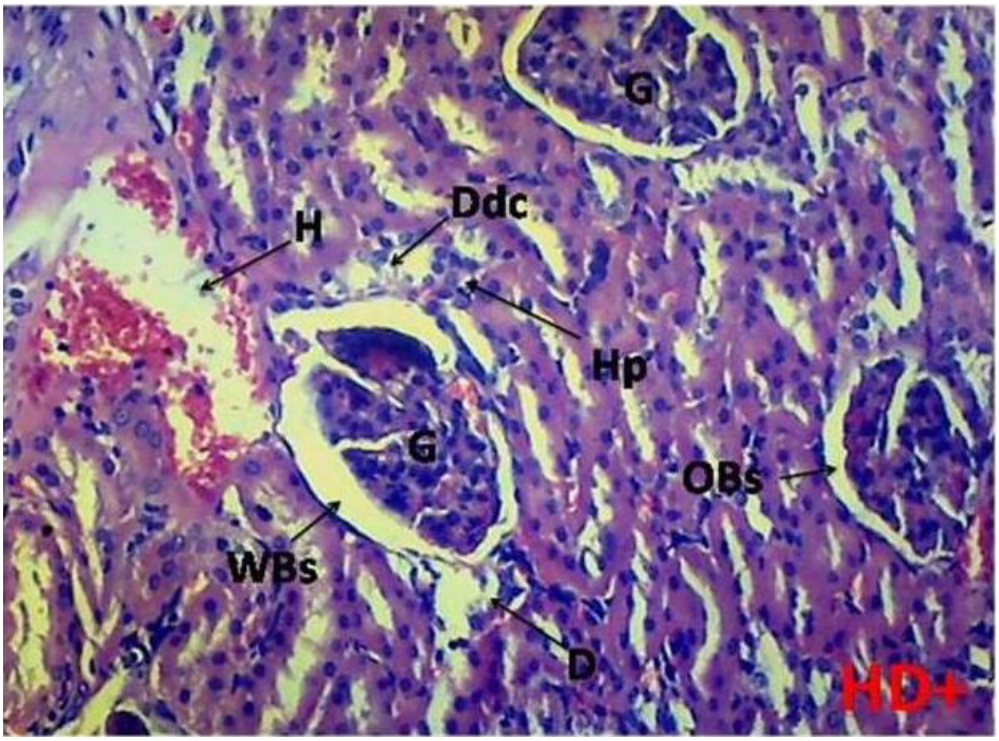

Plate 10. Photomicrograph of the transverse section of the kidney of the Higher dose (HD+) animal treated with 518mg/kg (40% of LD_{50}) of ethanol extract of *Xylopia aethiopica* fruit showing the nephrotic cortical area with degenerating glomeruli having widened and occluding Bowman spaces (WBs and OBs), degenerating ductal cells (Ddc) connective tissue degeneration (D) and hemorrhagic blood tissue (H) within the renal tissue. Mag.x100(H&E).

Effect of Ethanol Extract of *Xylopia aethiopica* on the Stomach of an Adult Wistar Rats

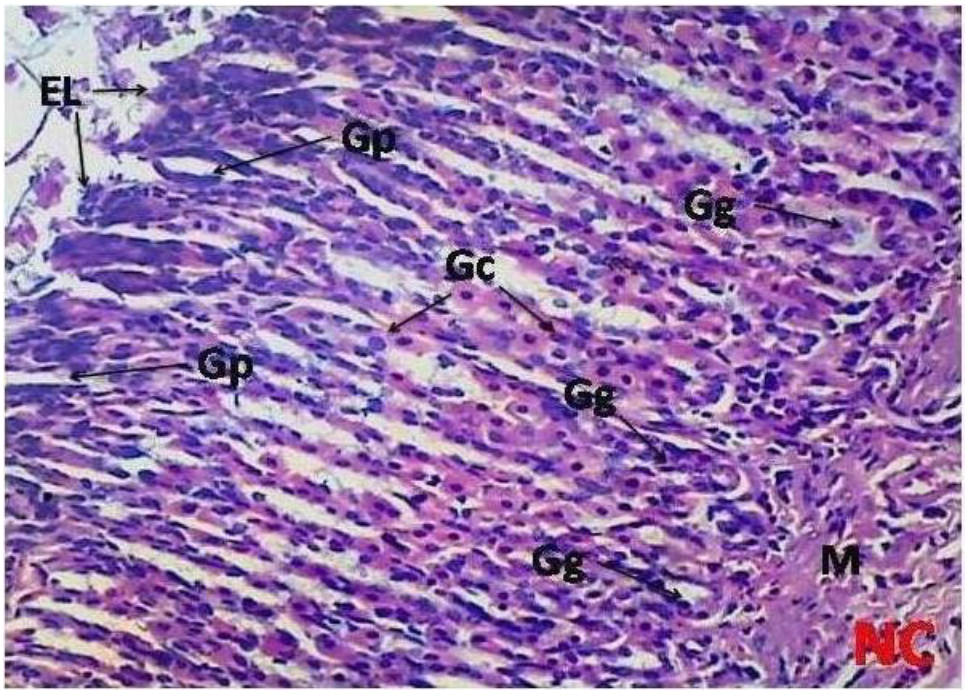

Plate 11. Photomicrograph of the transverse section of the stomach tissue of the Normal control group (NC) showing the gastric mucosa (M) with normal rays of gastric pits (GP), well arranged gastric cells (Gc) gastric glands (Gg) and the protected brush border of the epithelial layer (Ep). Mag.x100(H&E).

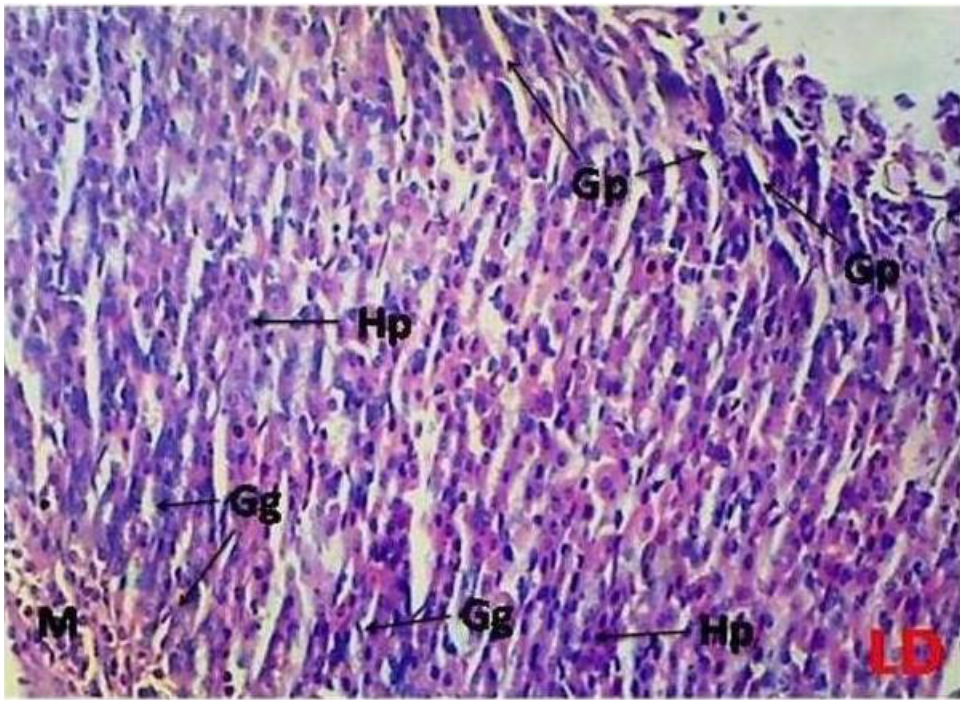

Plate 12. Photomicrograph of the transverse section of the stomach tissue of the low dose (LD) animal treated with 130 mg/kg (10% of LD_{50}) of ethanol extract of *Xylopia aethiopica* fruit showing the gastric mucosa (M) with rays of gastric pits (Gp) areas of gastric glands with some areas of hyperplastic gastric cells (Hp). Mag.x100 (H&E).

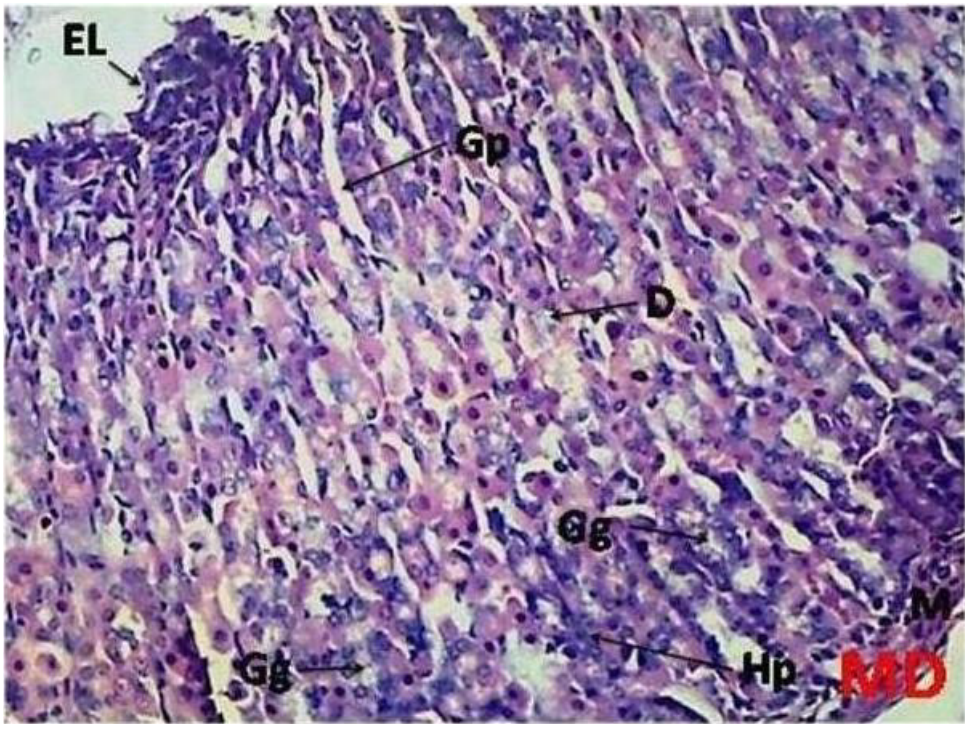

Plate 13. Photomicrograph of the transverse section of the stomach tissue of the middle dose (LD) animal treated with 259 mg/kg (20% of LD_{50}) of ethanol extract of *Xylopia aethiopica* fruit showing the gastric mucosa (m) with mild distorted gastric pits (Gp), areas of gastric cellular degeneration (D), gastric glands (Gg) hyperplastic gastric cells (Hp) and the epithelial layer (EL). Mag. x100(H&E).

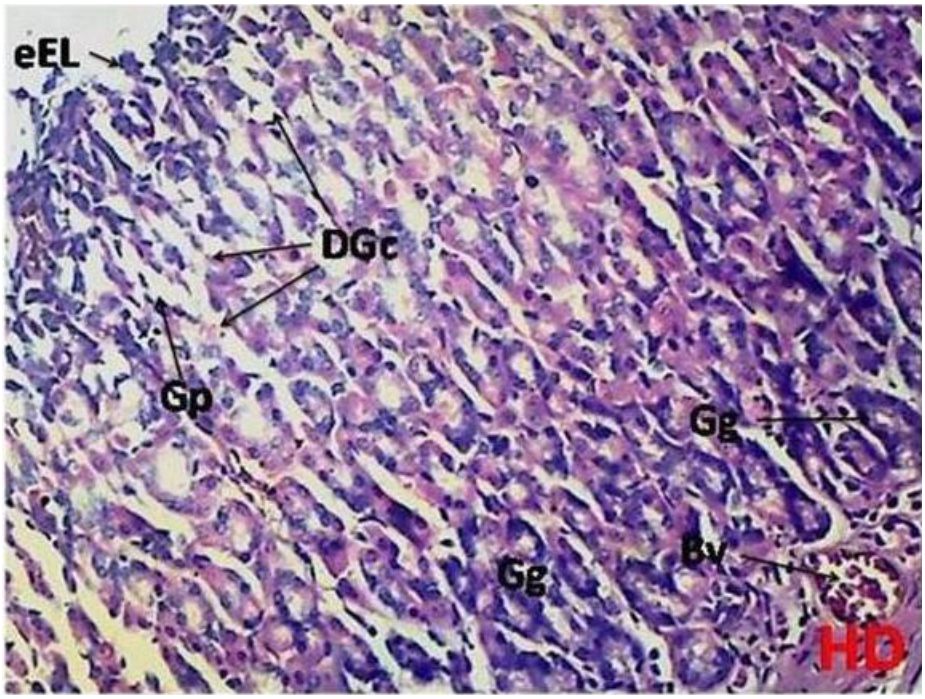

Plate 14. Photomicrograph of the transverse section of the stomach tissue of the High dose (HD) animal treated with 389mg/kg (30% of LD50) of ethanol extract of *Xylopia aethiopica* fruit showing the gastric mucosa (M) with wide areas of degenerating gastric cells (DGc), disorientation of the gastric pits (Gp), gastric glands, blood vessel (Bv) and eroding epithelial layer (eEL). Mag.x100 (H&E).

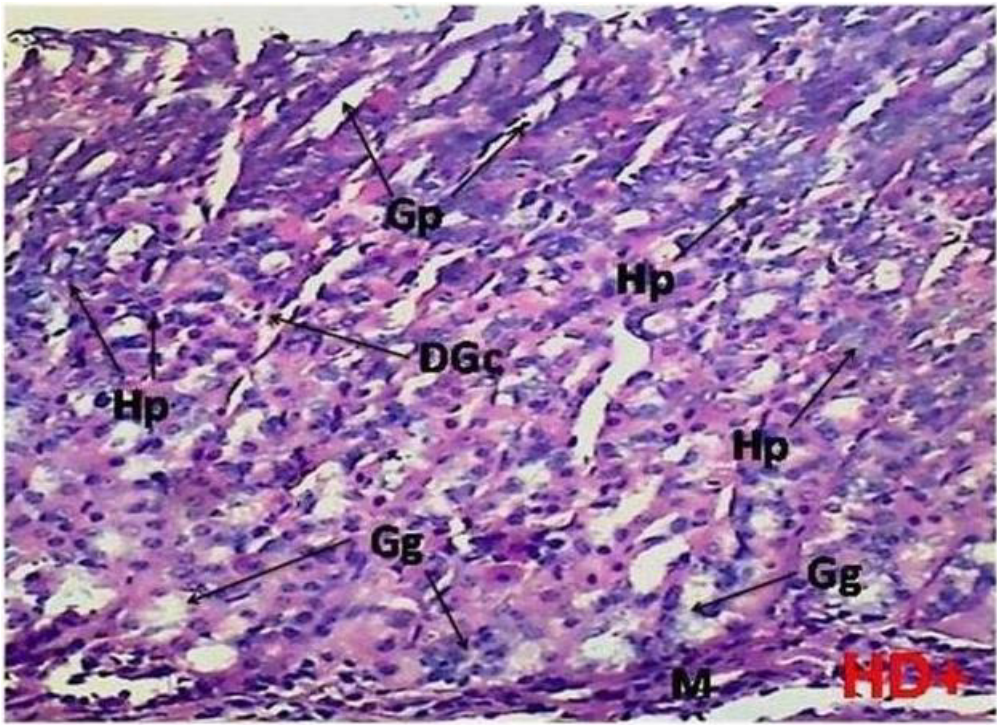

Plate 15. Photomicrograph of the transverse section of the stomach tissue of the Higher dose (HD+) animal treated with 518 mg/kg (40% of LD_{50}) of ethanol extract of *Xylopia aethiopica* fruit showing the gastric mucosa (M) with disoriented gastric pits (Gp), degenerating gastric cells (DGc), wide areas of hyperplastic gastric cells and the gastric gland (Gg). Mag.x100 (H&E).

Effect of Ethanol Extract of *Xylopia aethiopica* Fruit on the Heart of an Adult Wistar Rat

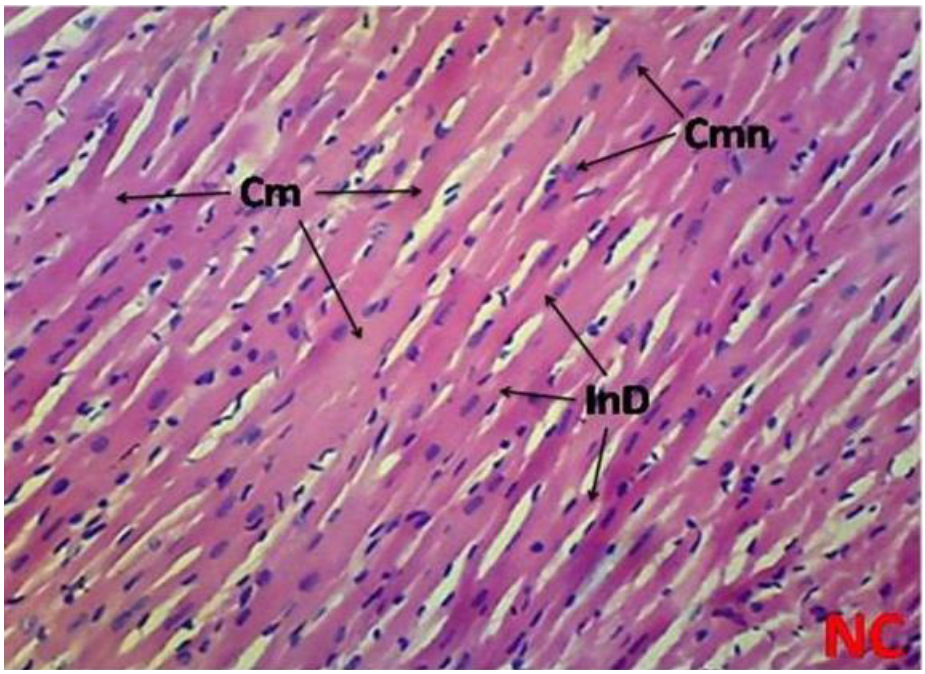

Plate 16. Photomicrograph of the longitudinal section of the right ventricular tissue of the heart of Normal control (NC) animals showing the cardiac tissue with well-presented cardiac myocytes (Cm), numerous cardiac myocyte nuclei (Cmn), and adjoining Intercalated disc of the cardiac muscle fibres. Mag.x100 (H&E).

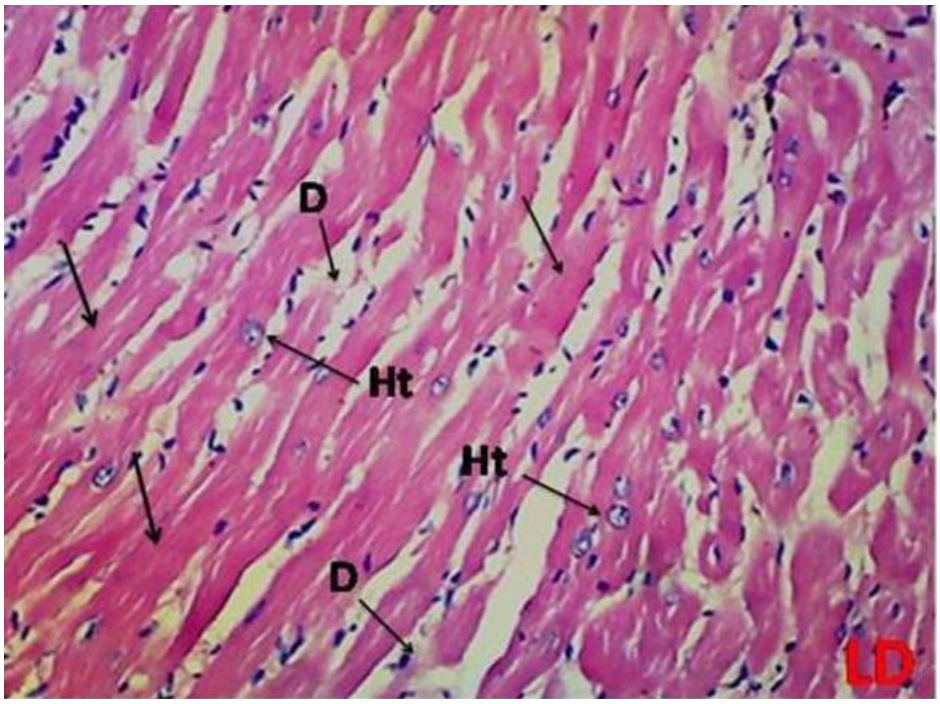

Plate 17. Photomicrograph of the longitudinal section of the right ventricular tissue of the heart of Low dose (LD) animal treated with130 mg/kg (10% of LD_{50}) of ethanol extract of *Xylopia aethiopica* fruit showing the cardiac tissue with areas of degenerating cardiac myocytes (D), hypertrophying cardiac myocyte nuclei (Ht), and areas of loss of myocyte nuclei (Arrow) within the cardiac muscle fibres. Mag. x100 (H&E).

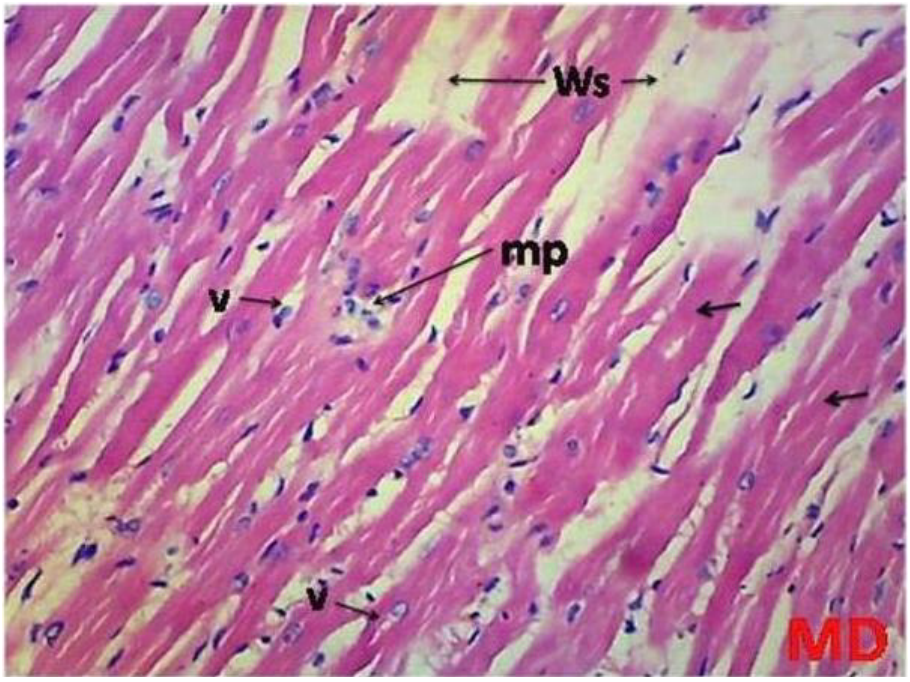

Plate 18. Photomicrograph of the longitudinal section of the right ventricular tissue of the heart of Medium dose (MD) animal treated with 259 mg/kg (20% of LD_{50}) of ethanol extract of *Xylopia aethiopica* fruit showing the cardiac tissue with areas of wide inter-fibre spaces (Ws), vacoulated cardiac myocyte (v), presence of macrophagic cells (mp) and areas of loss of myocyte nuclei (Arrow) within the cardiac muscle fibres. Mag. X100(H&E)

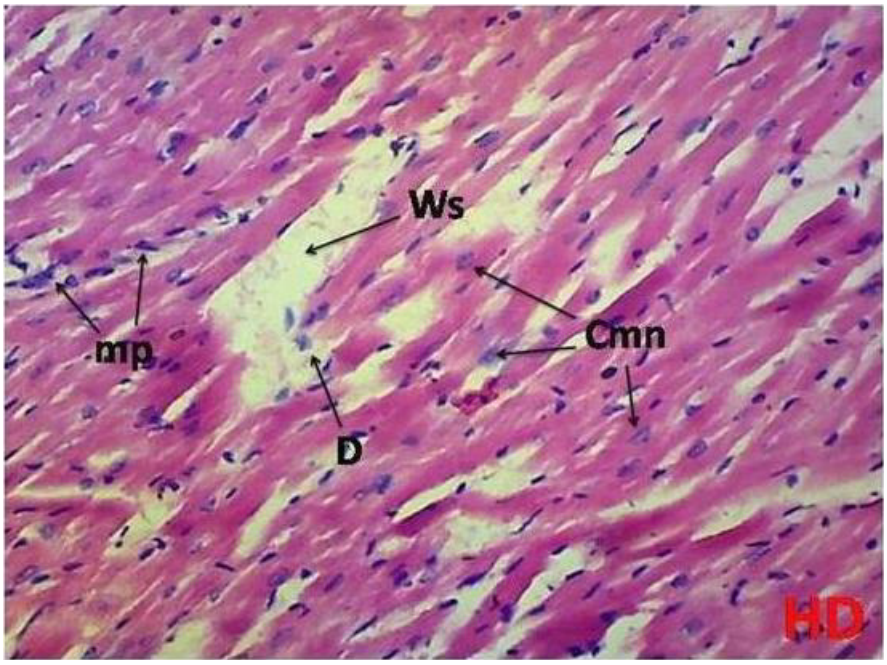

Plate 19. Photomicrograph of the longitudinal section of the right ventricular tissue of the heart of High dose (HD) animal treated with 389 mg/kg (30% of LD_{50}) of ethanol extract of *Xylopia aethiopica* fruit showing the cardiac tissue with numerous cardiac myocyte nuclei (Cmn), areas of wide inter-fibre spaces (Ws), presence of macrophagic cells (mp) and disorientation of the cardiac muscle fibres. Mag.X100 (H&E)

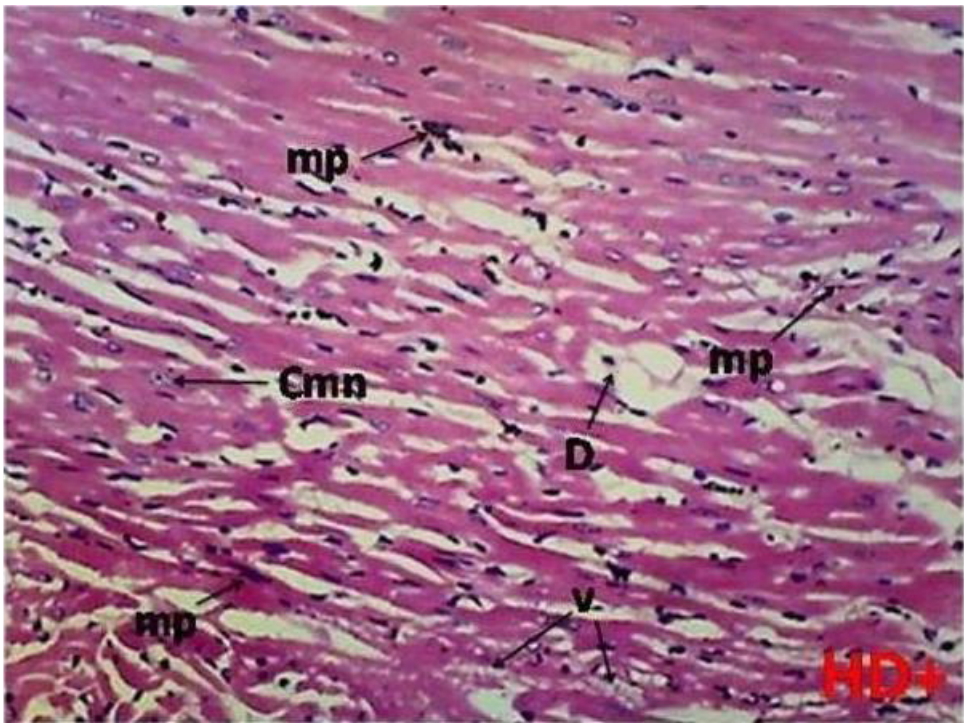

Plate 20. Photomicrograph of the longitudinal section of the right ventricular tissue of the heart of Higher dose (HD+) animal treated with 518.85mg/kg (40% of LD50) of ethanol extract of *Xylopia aethiopica* fruit showing the cardiac tissue with numerous cardiac myocyte nuclei (Cmn), vacuolated cardiac myocyte (v), presence of macrophagic cells (mg) and disorientations of the cardiac muscle fibres. Mag. x100(H&E)

Effect of Ethanol Extract of *Xylopia aethiopica* Fruit on the Testis of an Adult Wistar Rat

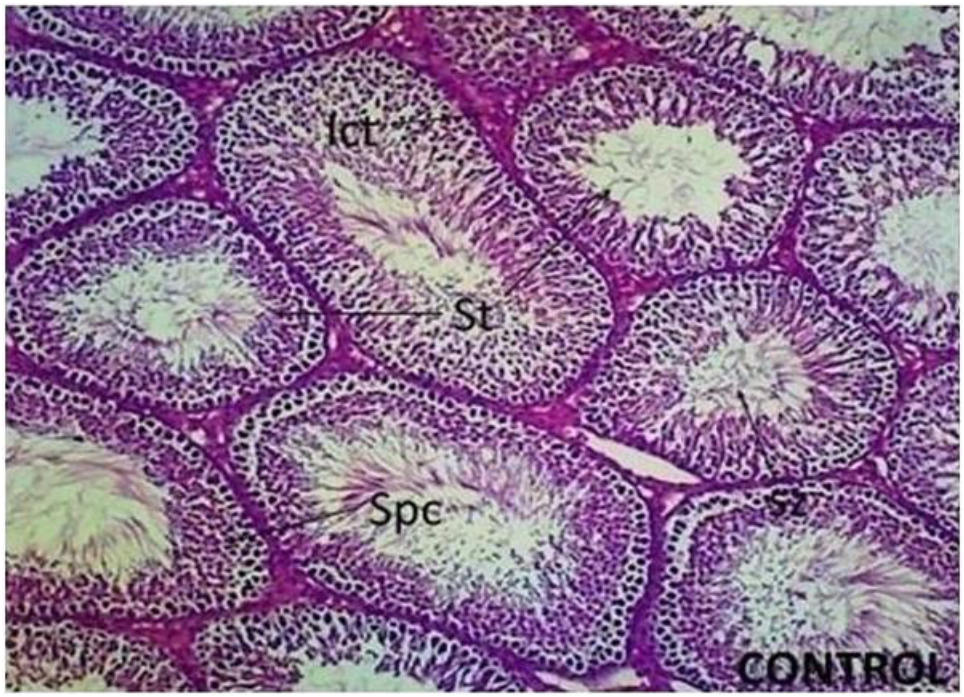

Plate 21. Photomicrograph of the section of the control testis showing normal cytostructure of the semiferrous tubules, well protected spermatogemic cells(Spc), well lined basement layer (BL) and, radiating spermatids (St) and spermatozoa (Sz), and well-presented cells within the interstitial connectives tissues (Ict).Mag. X100 (H & E).

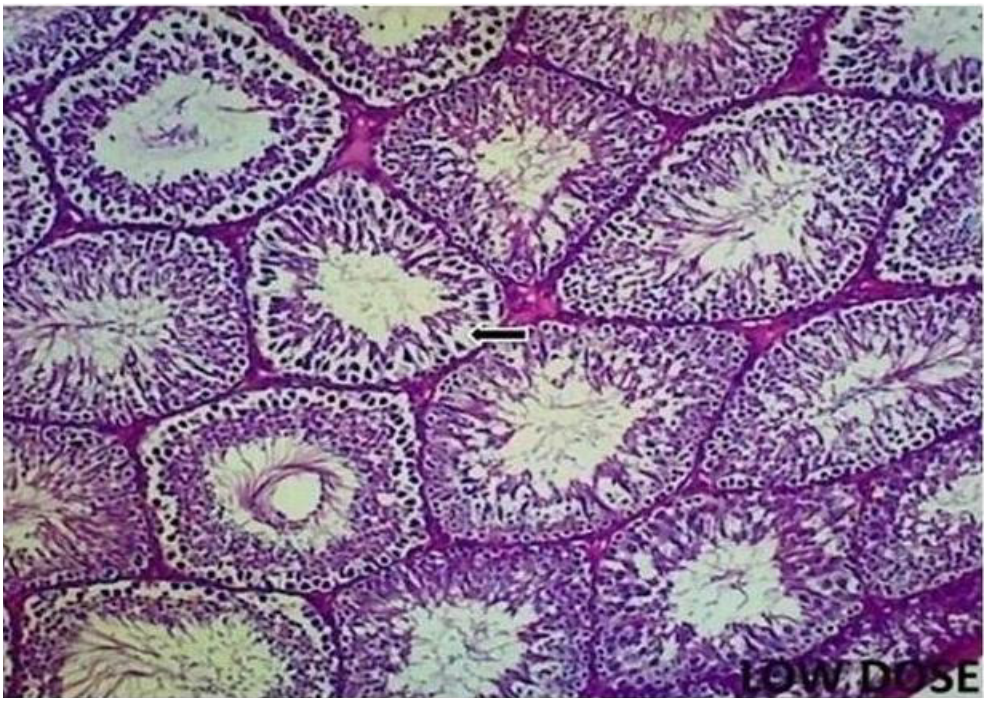

Plate 22. Photomicrograph of the transverse section of the testis of animals treated with 130 mg/kg (10% of LD_{50}) of *X. aethiopica* fruit showing seminiferous tubular architecture with presence of the spermatogenic cells, tubules with low radiating spermatozoa, and areas of degenerating spermatogenic cells (black arrow).Mag. x100 (H & E).

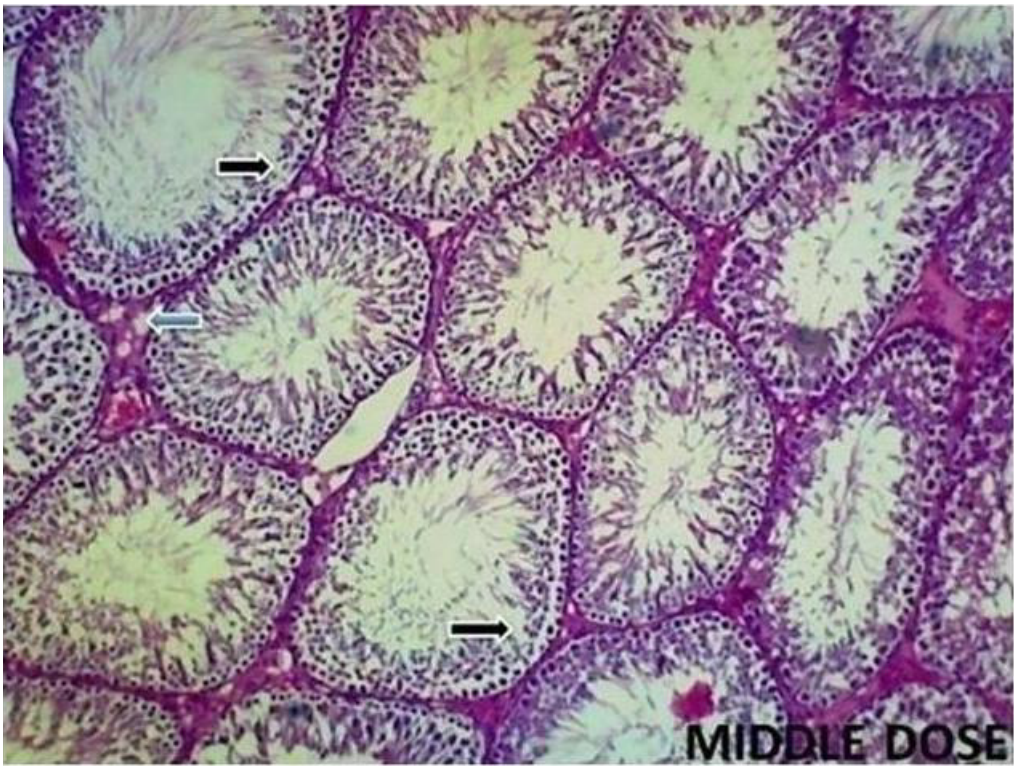

Plate 23. Photomicrograph of the transverse section of the testis of animals treated with 259 mg/kg (20% of LD_{50}) of *X. aethiopica* fruit showing seminiferous tubules with areas of widen tubular lumen and degenerating spermatogenic cells (Black arrow), and lipid droplets(Blue Arrow), within the interstitial connective tissues spaces. Mag. x100 (H & E).

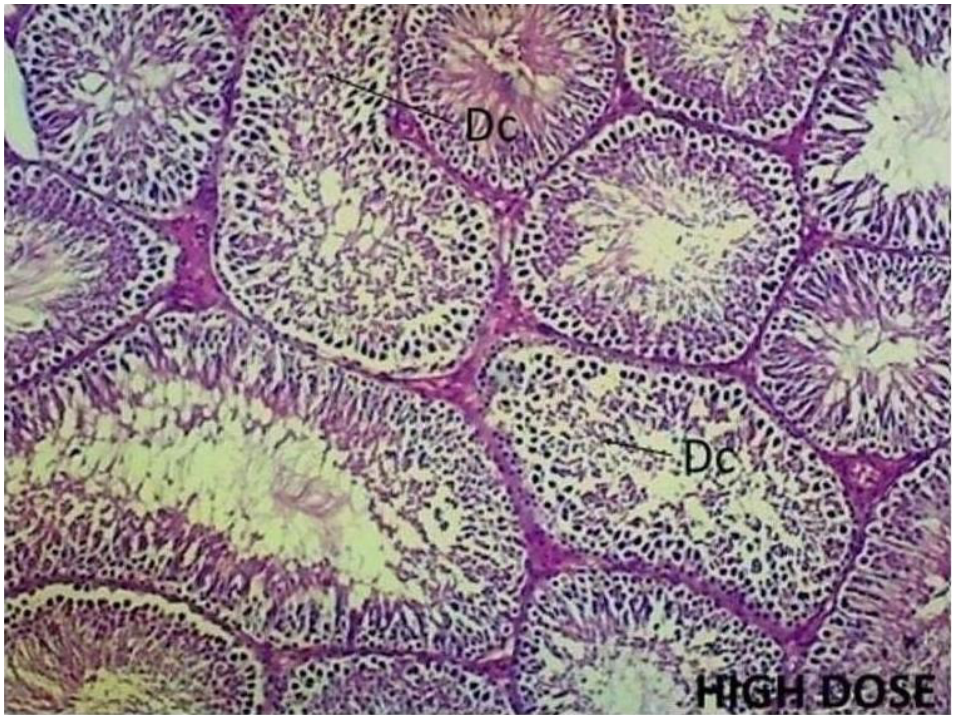

Plate 24. Photomicrograph of the transverse section of the testis of animals treated with 389 mg/kg (30% of LD_{50}) of *X. aethiopica* fruit showing abnormally distended seminiferous tubules with areas of displacements of the radiating spermatogenic cells (Dc), and widened tubular lumen with low spermatozoa. Mag. x100 (H & E).

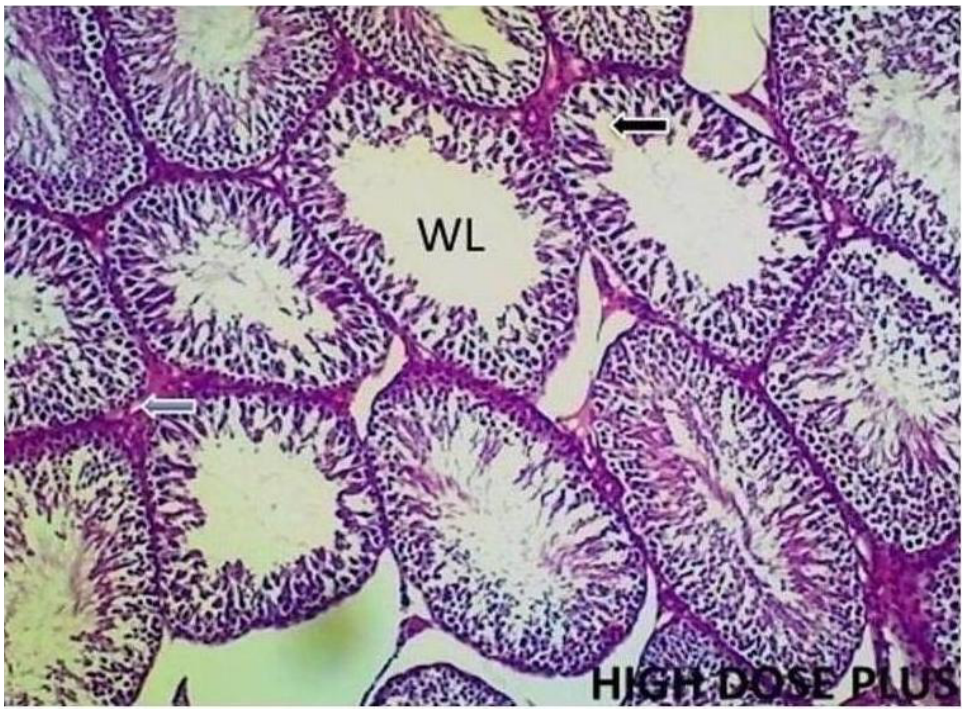

Plate 25. Photomicrograph of the transverse section of the testis of animals treated with 518 mg/kg (40% of LD_{50}) of *X. aethiopica* fruit with histological presentation of abnormal seminiferous tubules having areas of degenerations of the radiating spermatogenic cells (Black arrow), widened tubular lumen (WL) with low spermatozoa and wide areas of lipid droplets (Blue arrow) within the interstitial connective tissues. Mag. x100 (H & E).

Effect of Ethanol Extract of *Xylopia aethiopica* Fruit on the Uterus of an Adult Wistar Rat

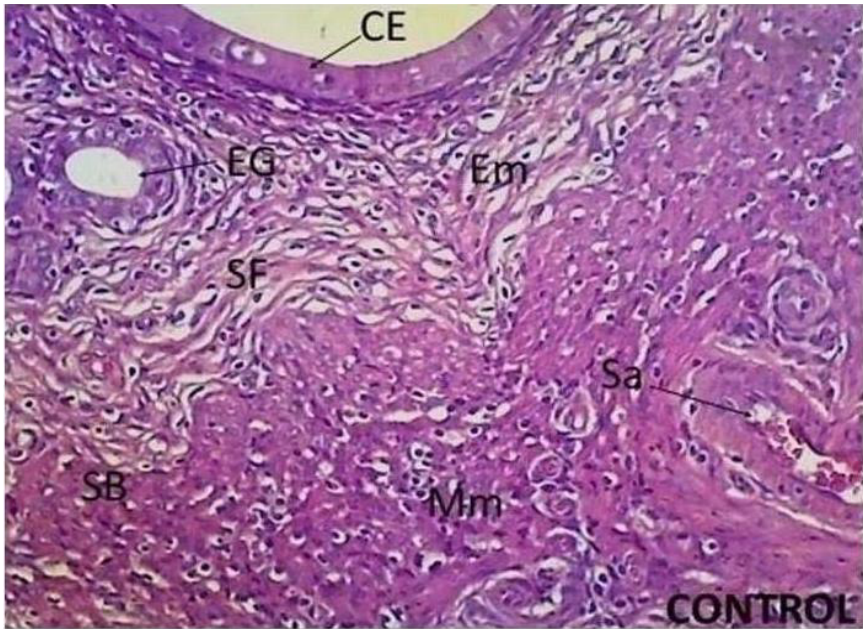

Plate 26. Photomicrograph of the section of the Control uterus showing the normal histoarchitecture with well-lined Columnar epithelium (CE), Endometrial gland (EG), Endometruim(Em) with well protected stratum functionalis (SF) and stratum basalis (SB), and presence of spiral arteries (SA) within the myometrium (Mm).Mag. x100 (H & E).

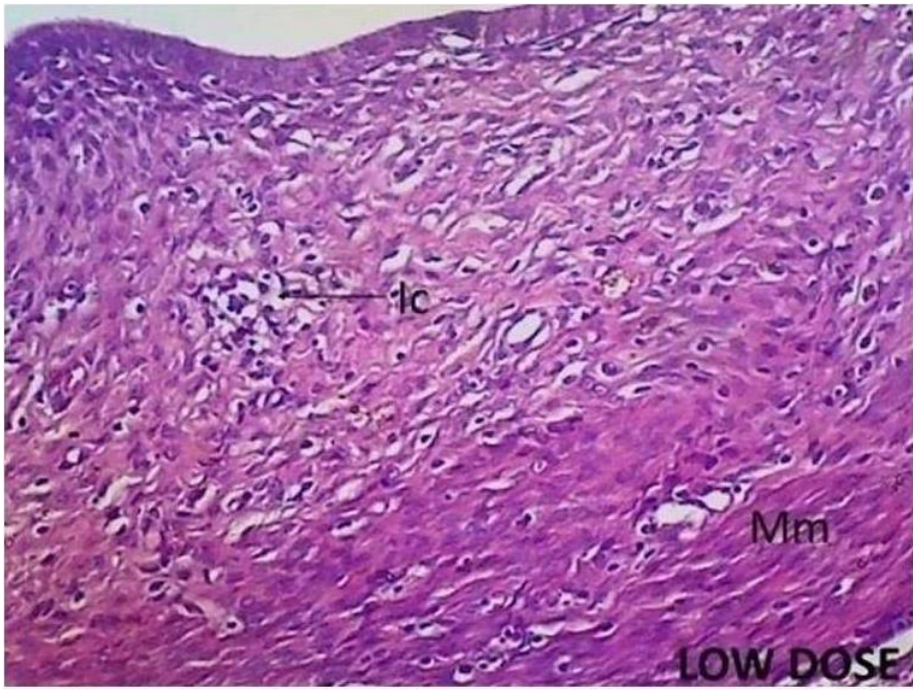

Plate 27. Photomicrograph of the section of the uterus of animals treated with 130 mg/kg (10% of LD_{50}) of *Xylopia aethiopica* fruit showing the uterine histostructure with well-lined Columnar epithelium of the endometruim and areas of inflammatory endometrial cells (Ic) with well protected myometrial layer (Mm). Mag. x100 (H & E).

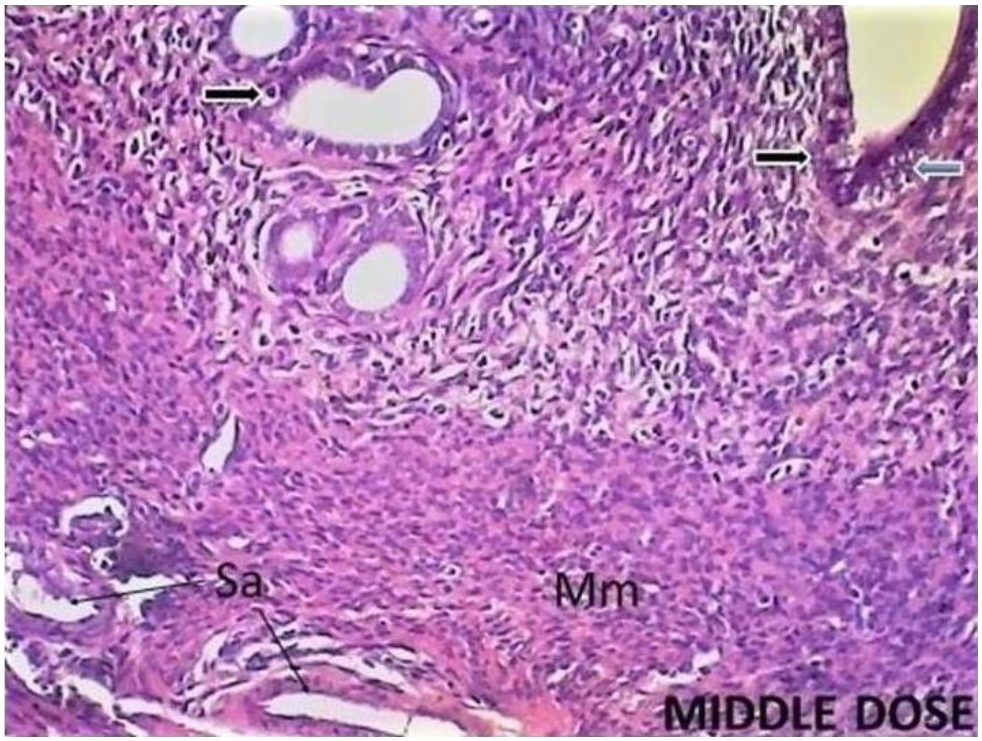

Plate 28. Photomicrograph of the section of the uterus of animals treated with 259 mg/kg (20% of LD_{50}) of *X. aethiopica* fruit showing the uterine cytoarchitecure with degenerating endometrial and vacoulatory glandular epithelial cells (Black arrow), infiltration of inflammatory cells (Blue arrow) and widened spiral arteries (Sa) within the myometruim (Mm).Mag. x100 (H & E).

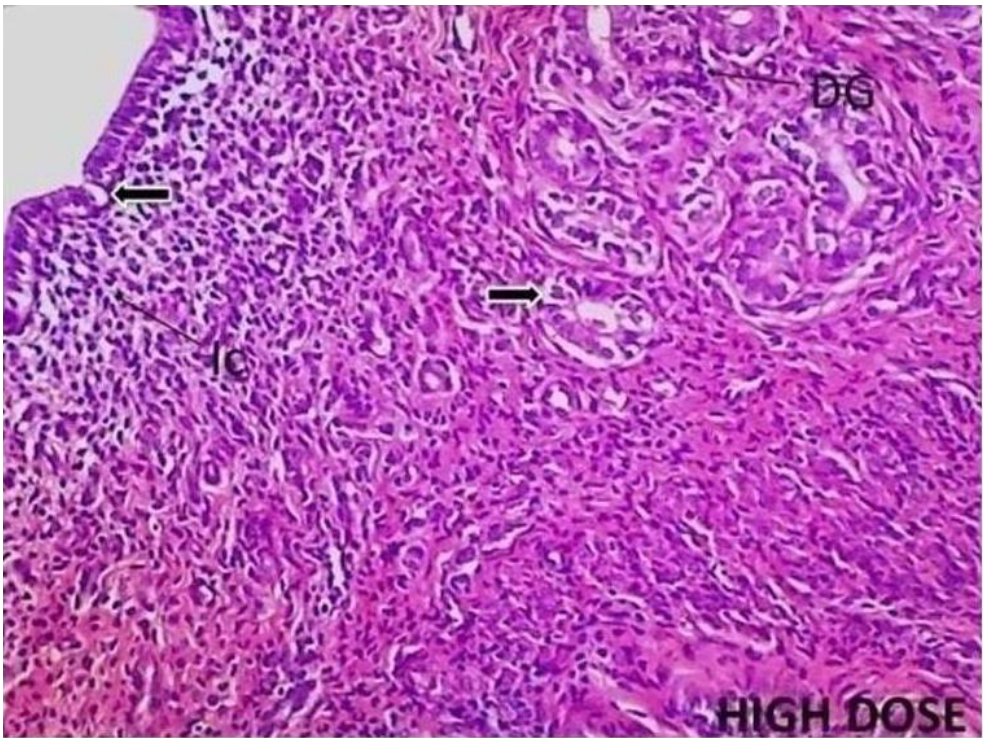

Plate 29. Photomicrograph of the section of the uterus of animals treated with 389mg/kg (30% of LD_{50}) of *X. aethiopica* fruit showing the uterine histostructure with degenerating endometrial columna lining cells and glandular epithelial cells (Black arrow), degraded gland (DG) and infiltration of inflammatory cells (Ic) within the uterine endometrium. Mag. x100 (H & E).

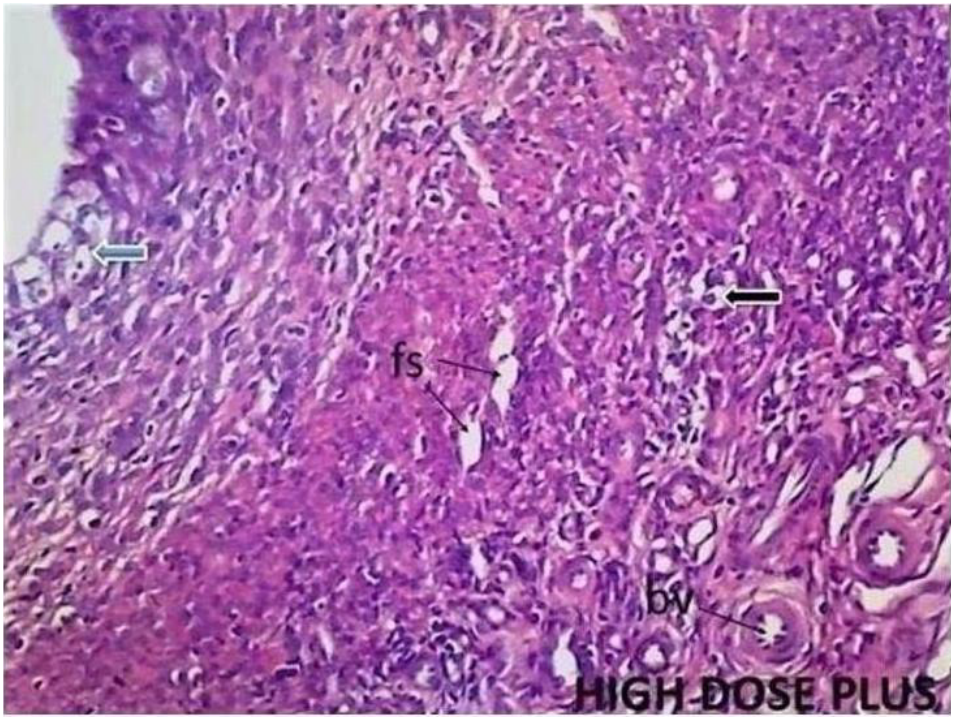

Plate 30. Photomicrograph of the section of the uterus of animals treated with 518 mg/kg (40% of LD_{50}) of *X. aethiopica* fruit showing the uterine histoarchitecture with degenerating and vacoulatory cells of the myometrium (Black arrow), hypertrophying and inflammatory columna epithelial cells (Blue arrow) and blood vessels (bv) and fluid space (fs) within the myometrial layer.Mag. X100 (H & E).

Effect of Ethanol Extract of *Xylopia aethiopica* Fruit on the Ovary of an Adult Wistar Rat

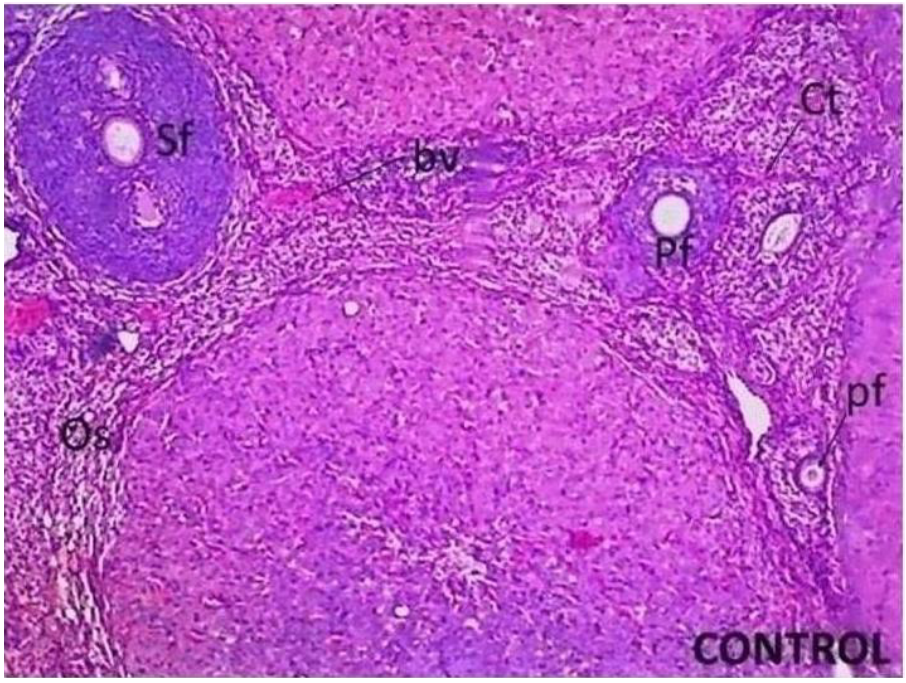

Plate 31. Photomicrograph of the section of the ovary control animals showing different levels of developing follicles, primordial follicle (pF) primary follicle (PF), secondary follicle (SF), wide spread blood vessels (bv), connective tissues (CT) and the Ovarian Stroma.Mag. x100 (H & E).

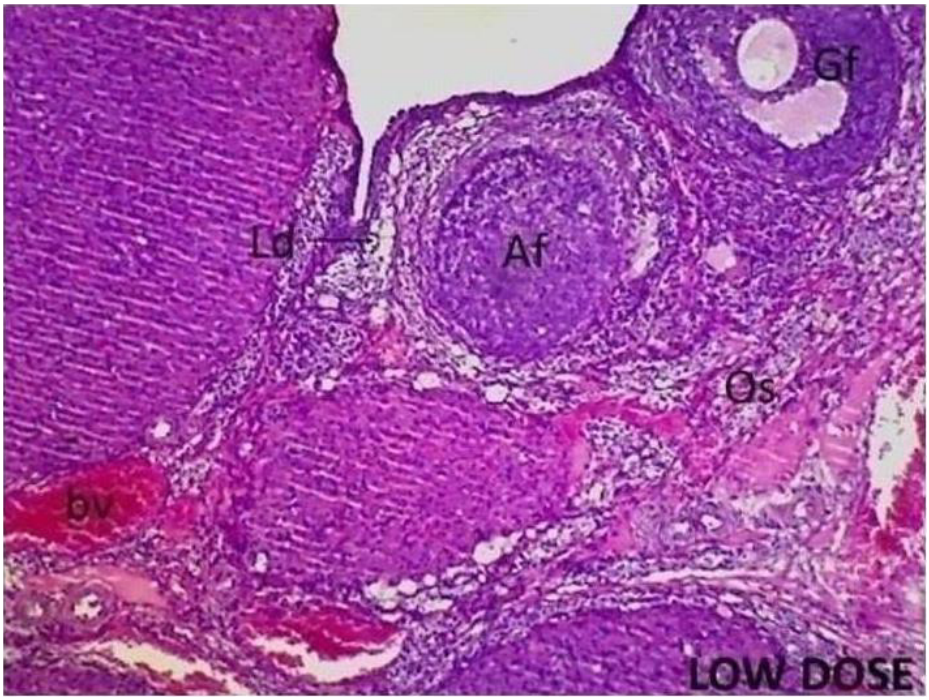

Plate 32. Photomicrograph of the section of the ovary of animals treated with 130 mg/kg (10% of LD_{50}) of *X. aethiopica* fruit showing the ovarian histoarhitecture with atrophying follicle (Af), Graffian follicle (Gf), widened blood vessels (bv), presence of lipid droplet (Ld) within the cortical stroma, and the ovarian stroma.Mag. X100 (H & E).

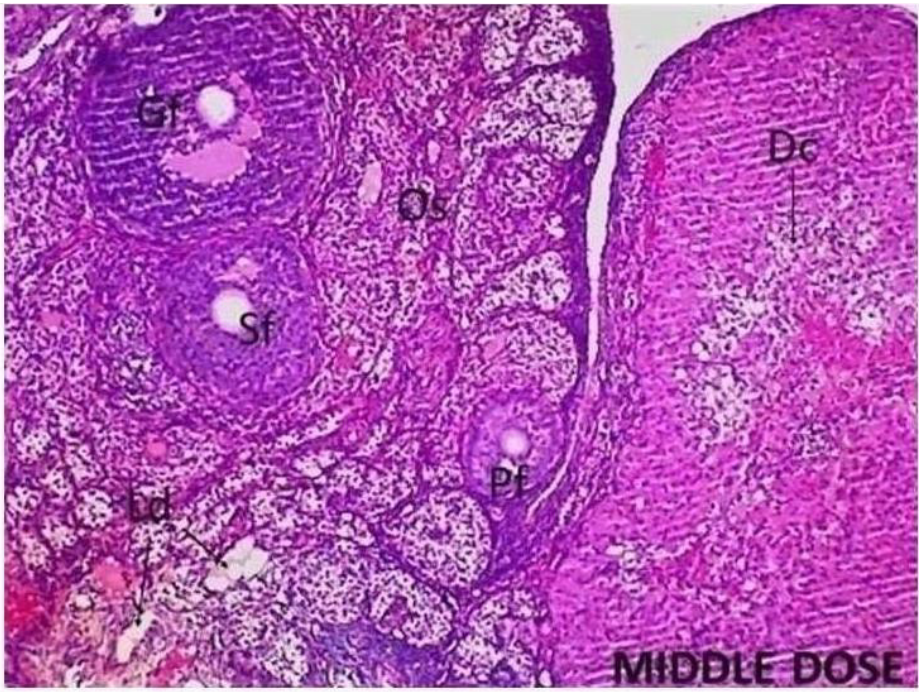

Plate 33. Photomicrograph of the section of the ovary of animals treated with 259 mg/kg (20% of LD_{50}) of *X. aethiopica* fruit showing the ovarian histostructure with developing follicles, primary follicles (Pf) secondary follicles (Sf) graffian follicle (Gf) and developing ovarian cyst (Dc) and presence of lipid droplet (Ld) within the cortical stroma. Mag. X100 (H & E).

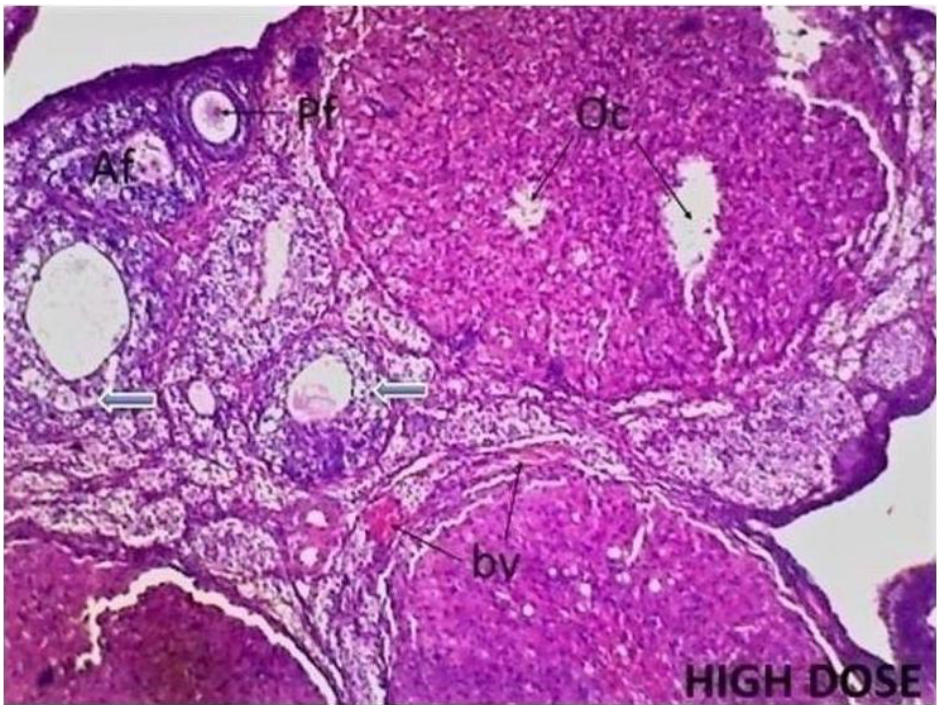

Plate 34. Photomicrograph of the section of the ovary of animals treated with 389 mg/kg (30% of LD_{50}) of *X. aethiopica* fruit showing the ovarian tissues with atrophying follicle (Af), primary follicle (Pf), degenerating follicular cells with accumulating fluid spaces (Blue arrow), Ovarian cyst and blood vessels within the ovarian stroma. Mag. x100 (H & E).

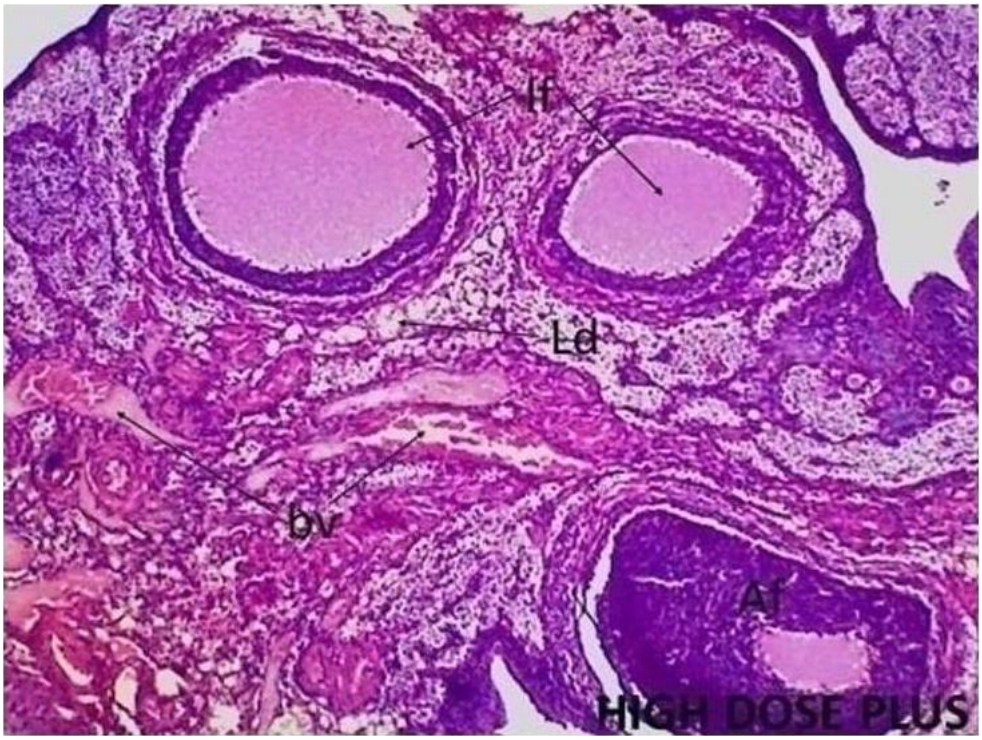

Plate 35. Photomicrograph of the section of the ovaryof animals treated with 518 mg/kg (40% of LD_{50}) of *X. aethiopica* fruit showing inflammation of the developing follicle (IF), lipid droplets (Ld), atrophying follicle and widened blood vessels within the cortical and ovarian stroma. Mag. x100 (H & E).

This is consistent with the destruction of sperm cells and total reduction of sperm qualities reported by Ogbuagu *et al*. (2022b) when they exposed animals to *Xylopia aethiopica* fruit for 28 days.

The Photomicrograph of a section of the uterus treated with high dose of ethanol extract of *Xylopiaaethiopica* fruit showed degeneration and vacoulatory cells of the myometrium, hypertrophying and inflammatory columna epithelial cells of the uterus. This implied that the extract has a significant adverse effect on the uterine cells of animals. This corroborated the toxic effect of the extract on female reproductive hormones observed by Ogbuagu *et al*. (2022c) when they administered ethanol extract of *Xylopia aethiopica* fruit to animals for 28 days. Consequently, the extract may impair fertility and conception in female. Thus, fruit extract of *Xylopia aethiopica* may be explored as a female contraceptive.

Photomicrographs of a section of ovary of rat treated with ethanol extract of *Xylopia aethiopica* fruit showed completely destroyed ovarian cell in a dose dependent manner especially with higher doses. It is probable that *Xylopia aethiopica* extract had adverse effect on the ovary and may be one of the factors causing female infertility following its varied use in the management of other medical conditions by alternative medical practitioners and rural dwellers.

CONCLUSION

The results of this study revealed that extract *Xylopia aethiopica* fruit destroyed the cells of tissues investigated thereby authenticating its toxicity.

Consent: It is not applicable.

Conflict of Interests: Authors declared that no conflict of interests exist in this study and publication.

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