# Dose-dependent effects of aqueous *Xylopia aethiopica* fruits extract on uterine apoptotic markers and placental histology in pregnant Wistar rats

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**ABSTRACT**

Apoptosis plays a critical role in uterine remodeling and placental development during pregnancy, with caspase-3 and caspase-8 serving as key regulatory enzymes. *Xylopia aethiopica* fruit (Ethiopian pepper) is widely used in African ethnomedicine, including during pregnancy, yet its effects on apoptotic pathways in gestation remain insufficiently characterized. This study investigated the effect of aqueous extract of *Xylopia aethiopica* fruit on uterine caspase-3 and caspase-8 levels and placental histology in pregnant Wistar rats during mid-gestation. Sixteen pregnant Wistar rats (150–180 g) were assigned into four groups (n = 4): control and extract-treated groups receiving 250, 500, or 1000 mg/kg body weight orally once daily from gestational days 8–14. Uterine tissues were analyzed for caspase-3 and caspase-8 levels using ELISA, while placental tissues were examined histologically using hematoxylin and eosin staining. Data were analyzed using one-way ANOVA with Bonferroni post hoc test at $p < 0.05$. The aqueous extract of *Xylopia aethiopica* produced a dose-dependent reduction in uterine caspase-3 and caspase-8 levels. Significant decreases were observed at 500 mg/kg and were more pronounced at 1000 mg/kg compared with the control group. Histological findings revealed preserved placental architecture in the control and low-dose groups, while moderate and high doses induced degeneration and necrosis of glycogen-rich cells within the labyrinth and junctional zones. *Xylopia aethiopica* aqueous extract modulates apoptotic activity in uterine tissues during mid-pregnancy in a dose-dependent manner. While low doses appear relatively safe, higher doses compromise placental integrity, indicating a narrow margin between therapeutic and toxic effects during pregnancy.

**Keywords:** *Xylopia aethiopica*; apoptosis; Caspase-3; Caspase-8; placenta; pregnancy.

## INTRODUCTION

Pregnancy is a dynamic physiological state characterized by tightly coordinated cellular, hormonal, and molecular events that support embryo implantation, placental development, and fetal growth (CHA et al., 2012). A key regulatory mechanism underlying these processes is apoptosis. Apoptosis is defned as a process of "programme cell death" durng which many cells simultaneously die within and along a very orderly/controlled pattern (BONGAERTS, 2008). PCD begins as soon as energy production within a cell or tissue becomes permanently insufficient to repress decay. Optimal energy production is required for optimal functioning of the cell. The factual cause factor of decay is limited energy production needed to conserve the structure of cells, tissues or organs eventually resulting in decay process which if becomes irreversible leads to the death of the cell (BONGAERTS, 2008). Decrease energy production which may result in decay may arise due to i) turning off of pivotal tricarbonic acid cycle, ii) turning off oxidative phosphorylation iii) Damage of mitochondria and iv) inhibition of mitochondrial biogenesis involving both mitochondrial and the nuclear part (BONGAERTS, 2008). Due to the decrease in energy production, massive inefficient fermentative energy with enormous amount of lactic acid results, leading to increasing acidity and decreased pH which slows down enzymatic activities and intracellular processes so that when energy for repair becomes insufficient cellular decay become irreversible and cell death results (BONGAERTS, 2008). Apoptosis can be classified based on the distinct morphological features in the tissue into three types: Type I which is recognized by cell rounding, DNA fragmentation, externalization of phosphatidyl serine, capase activation and absence of inflammatory reaction, Type II or autophagy is characterized by the presence of large vacuoles and the fact that the cells can recover until very late in the process and Type III (necrosis) which is associated with an uncontrolled release of intracellular content after cell swelling and rupture of the membrane which commonly induces and inflammatory response (SUZANNE & STELLAR, 2013).

Apoptosis is executed primarily by caspases, a family of cysteine-aspartic acid proteases enzymes synthesized as inactive zymogens and activated through tightly regulated signaling cascades (ADAMS & CORY, 2002). Caspases are master regulators of PCD, inflammation and immune responses. Caspases are activated in response to apoptotic signals and are broadly classified into initiator caspases (-8, -9) which starts the apoptotic process by responding to the death signals (extrinsic or death receptor and intrinsic or mitochondrial

pathways of apoptosis) and executioner or effector caspases (-3, -7) which are activated by initiator caspases and actively degrade structural proteins and nuclear components resulting in cell destruction (DANIEL & KORSMEYER, 2004; RAI et al., 2005). Among these, caspase-3 serves as a major executioner caspase, while caspase-8 functions as a key initiator in the extrinsic apoptotic pathway. In reproductive tissues, apoptosis, a genetically programmed form of cell death is essential for tissue remodeling, immune tolerance, and maintenance of placental homeostasis during gestation (LIU & WANG, 2001). Apoptosis can either shape an organ by the simple elimination of cells that are no longer require without inducing tissue damage or participate in morphogenesis by inducing cellular re-organization in the surrounding tissue (SUZANNE & STELLAR, 2013). In a nutshell apoptosis can either generate a pulling force or act as a biological scissor to release neighboring tissue by progressively chipping off small fragment of unwanted tissue from the neighboring tissue eventually creating a form of tissue (tissue remodeling). In tissue remodeling which is the main purpose of apoptosis, excess cells are eliminated to review a new shape in the tissue (SUZANNE & STELLAR, 2013). However, the mammalian immune system discriminate between modes of cell death, with necrosis often resulting in inflammation and adaptive immunity, while apoptosis tends to be anti-inflammatory by preventing the development of immune responses and suppressing the activation of the maternal T- lymphocyte which would have otherwise develop immune response against the fetal allograft thereby promoting immune tolerance (JERZAK & BISCHOF, 2002; KAZAMA et al., 2008). Apoptosis function to maintain homeostasis in the placenta by maintaining structural integrity of the trophoblast villi and eliminating damage or aged trophoblast cells especially at the syncyntiotrophoblast which culminates in the release of apoptotic “syncytial knots” into the maternal circulation ensuring a balance at the maternal-fetal interface (JERZAK & BISCHOF, 2002).

*Xylopia aethiopica* (Dunal) A. Rich., commonly known as Ethiopian pepper, is an aromatic spice widely used in West and Central African ethnomedicine. In Nigeria, it is traditionally employed for postpartum recovery, uterotonic purposes, and treatment of inflammatory and infectious conditions (NWAFOR et al., 2024; MORAKINYO et al., 2025). Phytochemical investigations have shown that *Xylopia aethiopica* fruits contain a wide range of bioactive compounds, including flavonoids, phenolics, alkaloids, saponins, steroids, glycosides, and essential oils, many of which possess antioxidant and apoptosis-modulating properties (ADEFEGHA & OBOH, 2012; EBEGBONI et al., 2019).

Experimental evidence indicates that these phytochemicals may influence apoptotic signaling by scavenging reactive oxygen species, stabilizing mitochondrial membranes, and down-regulating caspase-3 and caspase-8 activation (MIDDLETON et al., 2000; EBEGBONI et al., 2019). Ribeiro et al. (2021) investigating the activation of caspase in gastric adenocarcinoma AGS cells by *Xylopia aethiopica*, reported that, hydro-ethanolic extract of the fruit of XA resulted in caspase –3 activation. Nguedia et al. (2025) reported an increase in caspase-3 activity in an in vivo research investigating the effect of ethanolic extract of XA fruits on breast adenocarcinoma. Given the critical role of apoptosis in placental development and pregnancy maintenance, understanding how aqueous extract of *Xylopia aethiopica* affects caspase activity during gestation is of scientific and clinical relevance. Despite several work done using XA fruit extracts, no work seems to have been done to investigate the effect of aqueous XA fruit extract on uterine caspase-3 level hence, this study therefore investigated the effect of aqueous extract of Ethiopian pepper on uterine caspase-3 and caspase-8 levels and placental histology in pregnant Wistar rats during mid-gestation.

## MATERIALS AND METHODS

*Plant Material, Identification and Extract Preparation*

Dried fruits of *Xylopia aethiopica* were purchased from New Benin Market, Edo State, Nigeria, and authenticated by Prof. A.H. Akinnibosun of the Department of Plant Biology and Biotechnology, Faculty of life Science, University of Benin and was given a voucher number: UBH - X348 and deposited at the Herbarium. The fruits were washed, air-dried for two weeks, and ground into coarse powder. Five hundred grams of the powdered sample were macerated in 1.25 L of distilled water for 24 hours with intermittent stirring. The mixture was filtered, and the filtrate was concentrated on a water bath at 40 °C under reduced pressure for three days to obtain a dried brown extract weighing 48 g, corresponding to a percentage yield of 9.6%. The extract was stored under refrigeration, and fresh solutions were prepared as required according to the work of Azekhumen and Ebomoyi (2024) with slight modification.

*Ethical Approval*

Ethical approval was sorted the Research Ethics Committee of the College of Medical Sciences, University of Benin with Ethical approval number CMS/REC/2025/820 was assigned.

*Determination of LD50 of aqueous extract of Xylopia aethiopica (XA) fruit*

The LD50 of the aqueous extract was determined according to LORK method of 1983 in two phases: in phase I nine rats were used which were randomly distributed into three groups of n = 3 rats each group was treated with varying doses (10,100 and 1000mg/kg) of reconstituted extract of XA fruit per body weight of rat and the rats were closely observed for 24 hours for sign and symptoms of toxicity. In phase II three rats were used and was divided into three groups of n = 1 rat per group and each were administered orally (1600, 2900 and 5000mg/kg) of reconstituted per body weight of the fruit extract of XA respectively and were observed for 24 hours for signs and symptoms of toxicity and thereafter, for 2 weeks for delay sign of toxicity such as death and then the dose of the extract that gave the least death was considered the lethal dose, the maximum dose with 0% mortality was recorded as Xmg/kg while the minimum dose with 100% mortality was recorded as Ymg/kg and the two values were used to calculate LD50 of the aqueous extract as follows :

LD50 = $\sqrt{xy}$

*Experimental Animals*

Sixteen (16) virgin female Wistar rats weighing 150–180 g were obtained and housed in standard plastic cages at the Department of Anatomy, University of Benin. The animals were maintained under standard laboratory conditions and treated in accordance with the National Institutes of Health guidelines for the care and use of laboratory animals (NIH, 1985). Rats were allowed to acclimatize for two weeks with access to standard feed and water ad libitum.

*Mating, Pregnancy Confirmation, and Grouping*

Female rats were cohabited with male rats in a 2:1 ratio. Pregnancy was confirmed by the presence of a vaginal plug or positive vaginal smear, and the day of confirmation was designated gestation day one (GD1). Pregnant rats in the mid-gestation period (G8–G14) were randomly assigned into four groups (n = 4 per group):

- Group A (Control): Received standard feed and water only
- Group B (Low dose): Received 250 mg/kg body weight of extract
- Group C (Middle dose): Received 500 mg/kg body weight of extract
- Group D (High dose): Received 1000 mg/kg body weight of extract

The extract was administered orally once daily using a gavage for seven consecutive days (G8–G14).

*Sample Collection*

Twenty-four hours after the final administration, rats were weighed and sacrificed under chloroform anesthesia. Uterine tissues were excised, homogenized in phosphate buffer solution, and centrifuged at 3600 rpm for 10 minutes to obtain supernatants for biochemical analysis. Placental tissues were fixed in 10% neutral buffered formalin for histological examination according the work of Koneri et al. (2006) and Azekhumen & Ebomoyi (2024).

*Biochemical Analysis*

Uterine caspase-3 and caspase-8 levels were determined using standard ELISA-based assay procedures according to manufacturer' instruction.

*Histological Examination*

Fixed placental tissues were processed using standard histological techniques, embedded in paraffin, sectioned, and stained with hematoxylin and eosin (HandE) for light microscopic evaluation (BANCROFT & GAMBLE, 2006).

*Statistical Analysis*

Data were analyzed using GraphPad Prism version 10.6.1 and expressed as mean ± standard error of mean (SEM). Group comparisons were performed using one-way analysis of variance (ANOVA) followed by Bonferroni post hoc test. Statistical significance was set at $p < 0.05$.

**RESULTS**

LD50 Result: In phase I the only sign of toxicity observed after 24hrs was mild itching, and dizziness and in phase II after two weeks of administration of the fruit extract the only sign of toxicity observed was itching, dizziness, shivering, restlessness, frequent urination and mild loss of appetite but no death was recorded this lead to the establishment of the LD50 of the aqueous extract of the fruit of XA to be greater than 5000mg/kg and 10% of the LD50 was taken as the middle dose.

*Effect of Xylopia aethiopica Extract on Uterine Caspase-3 Levels.*

The mean uterine caspase-3 level in the control group was 0.8915 ± 0.04856. Rats treated with 250 mg/kg extract showed a reduced mean value of 0.7955 ± 0.02858, although this decrease was not statistically significant when compared with the control. In contrast, administration of 500 mg/kg resulted in a significant reduction in caspase-3 levels (0.7000 ± 0.02352; $p < 0.05$), while the 1000 mg/kg group exhibited a more pronounced decrease (0.6290 ± 0.04188; $p < 0.01$). A significant difference was also observed between the low- and high-dose groups, indicating a clear dose-dependent suppression of caspase-3 activity (Table 1).

**Table 1.** Caspase 3 Activity Across Experimental Groups.

| Group | Mean ± SEM | Significance |
|---|---|---|
| Control | 0.892 ± 0.049 | — |
| Low Dose (250 mg/kg) | 0.796 ± 0.029 | |
| Middle Dose (500 mg/kg) | 0.700 ± 0.024 | * |
| High Dose (1000 mg/kg) | 0.629 ± 0.042 | * |
| p-value (ANOVA) | **0.0016** | |

Note: Data are expressed as Mean ± SEM (n=4). *P < 0.05 compared with the control group based on Dunnett's post-hoc test following one-way ANOVA.

*Effect of Xylopia aethiopica Extract on Uterine Caspase-8 Levels.*

Uterine caspase-8 levels followed a similar dose-dependent pattern. The control group recorded a mean value of 0.7520 ± 0.03150. Treatment with 250 mg/kg produced a modest reduction (0.6925 ± 0.01245) that was not statistically significant. However, significant decreases were observed at 500 mg/kg (0.6503 ± 0.01321; $p < 0.05$) and at 1000 mg/kg (0.5470 ± 0.01856; $p < 0.001$) when compared with the control. These findings indicate progressive inhibition of the extrinsic apoptotic pathway with increasing extract dose (Table 2).

**Table 2.** Caspase 8 Activity Across Experimental Groups.

| Group | Mean ± SEM | Significance |
|---|---|---|
| Control | 0.752 ± 0.032 | — |
| Low Dose (250 mg/kg) | 0.693 ± 0.012 | |
| Middle Dose (500 mg/kg) | 0.650 ± 0.013 | * |
| High Dose (1000 mg/kg) | 0.547 ± 0.019 | * |
| p-value (ANOVA) | **<0.0001** | |

Note: Data are expressed as Mean ± SEM (n=4). *P < 0.05 compared with the control group based on Dunnett's post-hoc test following one-way ANOVA.

*Placental Histological Findings.*

Histological examination of placental sections from the control group revealed normal placental architecture with well-defined labyrinth and junctional zones and intact glycogen-rich cells. The low-dose (250 mg/kg) group largely preserved placental structure, showing minimal cellular distortion. In contrast, placentas from the 500 mg/kg group exhibited noticeable degeneration of glycogen cells within the junctional zone and areas of necrosis in the labyrinth zone. These alterations were more severe in the high-dose (1000 mg/kg) group, where marked necrosis, distortion of placental layers, and loss of normal labyrinthine architecture were observed (Figures 1 and 2).

Overall, the results demonstrate that aqueous extract of *Xylopia aethiopica* induces a dose-dependent reduction in uterine caspase-3 and caspase-8 levels during mid-pregnancy, accompanied by progressive placental structural damage at higher doses.

*Histology of the Placenta*

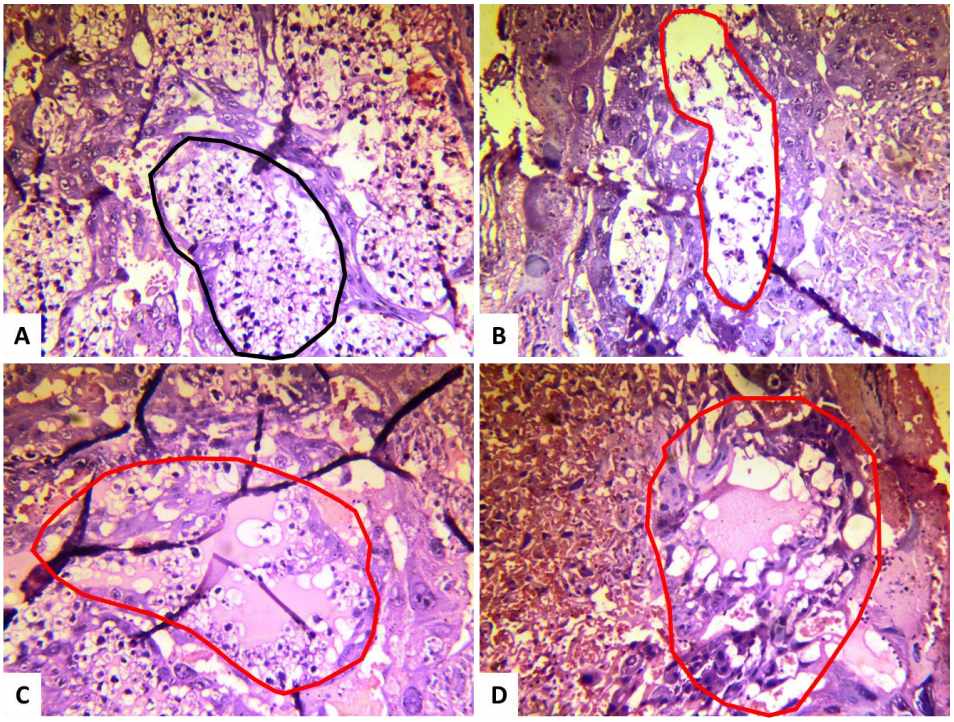


**Figure 1. PLATES A-D:** Photomicrographs of the junctional zone of the placenta (Hematoxylin and Eosin stain; ×100 magnification). **Plate A (Group A, control)** shows a normal junctional zone with well-defined glycogen cell islands (encircled black). **Plate B (Group B, 250 mg/kg)** demonstrates the presence of several degenerating cells within the glycogen cell islands (encircled red). **Plate C (Group C, 500 mg/kg)** similarly shows increased degeneration of cells within the glycogen cell islands. **Plate D (Group D, 1000 mg/kg)** reveals marked degeneration of glycogen cell islands, indicating progressive structural disruption with increasing doses of aqueous *Xylopia aethiopica* extract.

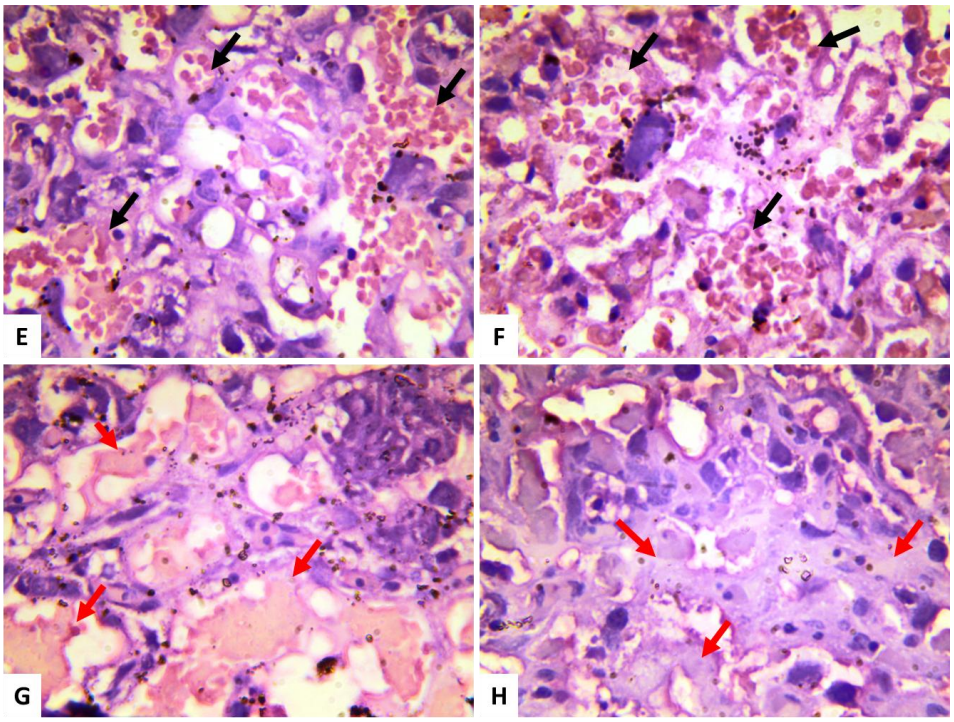


**Figure 2. PLATES E–H:** Photomicrographs of the labyrinth zone of the placenta (Hematoxylin and Eosin stain; ×400 magnification). **Plate E (Group A, control)** shows normal labyrinth architecture with numerous sinusoids filled with maternal and fetal blood (black arrow). **Plate F (Group B, 250 mg/kg)** similarly demonstrates well-preserved labyrinth structure with several blood-filled sinusoids (black arrow). In contrast, **Plate G (Group C, 500 mg/kg)** reveals severe necrosis of the labyrinthine tissue (red arrow). **Plate H (Group D)** also shows marked necrosis of the labyrinth zone (red arrow), indicating progressive structural damage at higher doses of aqueous *Xylopia aethiopica* extract.

## DISCUSSION

The present study investigated the effect of aqueous extract of *Xylopia aethiopica* on uterine apoptotic markers and placental histology in pregnant Wistar rats during mid-gestation (G8–G14). The findings demonstrate a dose-dependent reduction in uterine caspase-3 and caspase-8 levels following extract administration. This finding agrees in part with the work of Ebegboni et al. (2019) who reported an inhibition of pro-apoptotic kinases (P38 MAPK activation and C-JUN-N-terminal kinase). The decrease in caspase-3 and 8 levels in the treated pregnant rats maybe as a result of flavonoid content in the extract of the fruit of XA. Dietary flavonoids (quercetin, hesperetin) and their metabolites either alone or in combination has been reported to significantly decrease the level of oxidative stress in human trophoblast through inhibition of excessive caspase-mediated apoptosis thereby enhancing trophoblast invasion in

early pregnancy (EBEGBONI et al., 2019). However, the dose and timing of the ingested flavonoid has been reported to complicate pregnancy as excessive flavonoid intake during pregnancy may result in pregnancy complications such as pre-eclampsia, intra-uterine growth restriction, pre-term pre-labor contraction, spontaneous miscarriages resulting in fetal-maternal mortality (EBEGBONI et al., 2019). The decrease in uterine caspase-3 and 8 protein level observed in this study, contradicts the fnding by Gholami et al. (2017) who reported that exposure of BALB/C mice to silymarin a flavonolignan, increased the susceptibility of BALB/C mice fetuses brain, kidney and heart to apoptosis by increasing caspase-3 and 8 protein levels. The difference in the caspase-3 and 8 protein levels observed in this study may be due to the doses administered, organ of study, age of the mice 'foetuses and duration of administration. The decrease in uterine caspase-3 and 8 level observed in this study was accompanied by corresponding alterations in placental morphology at higher doses. These observations suggest that *Xylopia aethiopica* fruit exerts significant modulatory effects on apoptotic pathways during pregnancy.

Caspase-3 is a key executioner caspase responsible for the terminal events of apoptosis, including DNA fragmentation and cellular dismantling, while caspase-8 functions as an initiator caspase in the extrinsic apoptotic pathway (LIU & WANG, 2001; ADAMS & CORY, 2002). In normal pregnancy, controlled suppression of apoptosis during mid-gestation is essential to support uterine remodeling, placental stability, and fetal growth (TAYLOR et al., 2008). The observed reduction in both caspase-3 and caspase-8 levels, particularly at the medium (500 mg/kg) and high (1000 mg/kg) doses, indicates that the aqueous extract of *Xylopia aethiopica* inhibits both initiation and execution phases of apoptosis within uterine tissues.

The anti-apoptotic effect observed in this study is consistent with the known phytochemical composition of *Xylopia aethiopica*. The fruit contains flavonoids, phenolics, alkaloids, saponins, glycosides, steroids, and essential oils, all of which have been reported to possess antioxidant and apoptosis-modulating properties (ADEFEGHA & OBOH, 2012; EBEGBONI et al., 2019). These compounds are known to scavenge reactive oxygen species, stabilize mitochondrial membranes, and down-regulate caspase activation, thereby reducing oxidative stress-induced apoptosis (MIDDLETON et al., 2000; EBEGBONI et al., 2019).

Since oxidative stress is a major upstream trigger of caspase activation during pregnancy, attenuation of oxidative damage may account for the reduced caspase activity observed in the treated groups.

The findings of this study align with previous reports demonstrating that *Xylopia aethiopica* extracts suppress markers of oxidative stress, inflammation, and apoptosis in experimental models (NGEDIA et al., 2025). However, contrasting findings have also been reported, where certain fractions or doses of *Xylopia aethiopica* increased caspase activity in hepatic or testicular tissues (ADIKWU & EHIGIATOR, 2020). These discrepancies highlight the tissue-specific and dose-dependent nature of the plant's biological effects, as well as the influence of extraction methods and duration of exposure.

Histological evaluation of the placenta further supports the biochemical findings while revealing important dose-related structural consequences. The control group exhibited normal placental architecture with intact labyrinth and junctional zones, consistent with healthy maternal–fetal exchange. The low-dose group largely preserved placental integrity, suggesting a protective or adaptive response at this concentration. In contrast, moderate and high doses produced progressive degeneration of glycogen-rich cells and necrosis within the labyrinth zone.

These alterations are critical, as the labyrinth zone is responsible for nutrient and gas exchange between mother and fetus, and damage to this region may compromise placental efficiency and fetal development.

The coexistence of reduced apoptotic markers and placental necrosis at higher doses suggests that excessive suppression of apoptosis may be detrimental during pregnancy (ZHANG et al., 2023). While controlled inhibition of apoptosis is necessary for tissue stability (HADIAN & STOCKWELL, 2023), complete or excessive suppression may interfere with normal placental cell turnover, leading to accumulation of damaged cells and subsequent tissue degeneration. This finding underscores the importance of tightly regulated apoptotic activity during gestation and indicates that the beneficial effects of *Xylopia aethiopica* are dose-limited.

Overall, the study demonstrates that aqueous extract of *Xylopia aethiopica* modulates uterine apoptotic pathways during mid-pregnancy, likely through antioxidant and anti-apoptotic mechanisms mediated by its phytochemical constituents. However, the placental structural damage observed at higher doses raises concerns regarding excessive consumption during pregnancy. These findings support traditional claims of the medicinal value of Ethiopian pepper while emphasizing the need for cautious dose regulation to avoid potential reproductive toxicity.

## CONCLUSION

Administration of aqueous extract of *Xylopia aethiopica* during mid-pregnancy (G8–G14) produced a dose-dependent reduction in uterine caspase-3 and caspase-8 levels in pregnant Wistar rats, indicating suppression of apoptotic activity. While low-dose exposure preserved placental architecture, higher doses were associated with placental degeneration and necrosis. These findings suggest that *Xylopia aethiopica* exhibits dose-dependent anti-apoptotic effects with a narrow safety margin during pregnancy, underscoring the need for cautious use.

## LIMITATIONS OF THE STUDY

Despite the relevance of the findings, certain limitations should be acknowledged:

1. Limited sample size: Each experimental group consisted of four animals, which may reduce statistical power and limit generalizability of the findings.
2. Restricted biomarkers: The study focused only on caspase-3 and caspase-8 as apoptotic markers. Other apoptosis-related proteins, oxidative stress markers, or inflammatory mediators were not assessed.
3. Lack of fetal outcome assessment: Parameters such as fetal weight, number of viable fetuses, resorption sites, or congenital anomalies were not evaluated, limiting conclusions on fetal safety.
4. Single extraction method: Only the aqueous extract of *Xylopia aethiopica* was investigated; other solvent extracts may exhibit different biological effects.
5. Short exposure window: The study was limited to mid-gestation (G8–G14), and effects during early or late pregnancy were not explored.

## RECOMMENDATIONS AND FUTURE DIRECTIONS

Based on the findings and identified limitations, the following recommendations are proposed:

1. Future studies should include larger sample sizes to strengthen statistical robustness and improve translational relevance.
2. Expanded biochemical profiling, including oxidative stress markers, inflammatory cytokines, and additional apoptotic regulators, should be

incorporated to better elucidate mechanisms of action.

3. Fetal outcome parameters should be assessed to determine the implications of placental damage on fetal development and pregnancy outcomes.
4. Comparative studies using different extraction solvents and phytochemical fractions are recommended to identify the specific compounds responsible for the observed effects.
5. Longitudinal studies examining early, mid, and late gestational exposure would provide a more comprehensive understanding of gestational stage-specific effects.

## IMPLICATIONS OF THE STUDY

The findings of this study have important implications for reproductive biology and public health. They provide experimental evidence that *Xylopia aethiopica* possesses bioactive properties capable of modulating apoptotic signaling in reproductive tissues during pregnancy.

While low doses may support uterine and placental stability, high doses pose a risk of placental damage, emphasizing the importance of dose regulation.

Given the widespread traditional use of Ethiopian pepper among pregnant women in some communities, these results highlight the need for scientific guidance on its safe use during pregnancy. The study contributes valuable data to the growing body of literature on plant-derived modulators of apoptosis and underscores the necessity for caution when translating ethnomedicinal practices into clinical or dietary recommendations.

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