Tropical Journal of Drug Research March 2025; 2 (3): 64 - 69
ISSN: 2476-8065 (Electronic)
Available online at http://www.tjdr.org
https://doi.org/10.26538/tjdr/v2i3.1

Original Research Article

Evaluation of Associated Changes on the Uterus and Fallopian Tube Histology in Response to Graded Doses of *Syzygium aromaticum* (Clove) in Wistar Rats

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Sent for review: 09 February 2025 Revised accepted: 21 March 2025

Abstract

Purpose: *Syzygium aromaticum* (Clove) is used as a preservative, as well as in the preparation of various spicy foods. This study aimed to evaluate the effect of graded doses of cloves on the uterus and fallopian tube histology using Wistar rats as experimental animal model.

Method: Twenty (20) Wistar rats after two weeks of acclimatization were assigned into four groups (I, II, III and IV) of five animals each. Group I served as the control group and received normal saline, while Groups II, III, and IV received 2 mL, 4 mL, and 6 mL of clove extract once daily for 30 days. The body weights of the rats were monitored over the treatment period. At the end of the experimental period, the animals were fasted for 12 hours and thereafter were sacrificed, and their uterus and fallopian tubes were harvested and used for histological examination.

Results: *Syzygium aromaticum* extract exhibited dose-dependent effect on the histoarchitecture of the female reproductive tissues, particularly, the uterus and fallopian tubes in Wistar rats. Low and moderate doses of the extract appeared to maintain normal tissue architecture, while high doses resulted in mild degenerative changes.

Conclusion: These findings suggest that a high dose of *Syzygium aromaticum* has the potential to cause mild structural changes in the histoarchitecture of the female reproductive tissues, particularly, the uterus and fallopian tube.

Keywords: *Syzygium aromaticum*, Uterus, Fallopian Tube, Histology, Wistar Rats

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INTRODUCTION

Syzygium aromaticum commonly called clove originated from Maluku Island in Indonesia but are now widely distributed in several regions around the world. Clove has been utilized in traditional Chinese medicine as a remedy for stomach ailments such as inflammation and diarrhea.[1-5] Cloves are also known for their strong and pungent aroma which is attributed to the presence of essential oil like eugenol. They have a warm, sweet and slightly bitter taste. In cooking, cloves are often used whole to add flavour to both sweet and savory dishes. They are commonly used in spices and are a popular ingredient in pickles, marinades and soups. In traditional medicine, cloves have been used for their analgesic, antiseptic, and antibacterial properties.[6-11] They are believed to help relieve toothaches, reduce inflammation, and improve digestion. Cloves are also known to have antioxidants properties which may help protect against oxidative stress and promote overall health.[12] Recent scientific research has highlighted potential health benefits of cloves. Studies have suggested that cloves may have antimicrobial, antifungal and antiviral properties. They may also have anti-inflammatory effects and could potentially aid in managing conditions like arthritis and respiratory disorders.

The uterus and fallopian tube are integral part of the female reproductive system. The uterus is also known as the womb, it is a hallow, muscular organ located in the female pelvis. It consists of three layers: the innermost layer called the endometrium; the middle layer called the myometrium and the outermost layer called the perimetrium.[13] The main function of the uterus is to support the development and growth of fertilized eggs during pregnancy.[14] It provides a nourishing environment for the embryo and helps in the formation of the placenta. If pregnancy dose not occurs, the lining of the uterus is shed during menstruation. The uterus is influenced by various hormones, including estrogen and progesterone. These hormones regulate the menstrual cycle, control the growth and shedding of the endometrium and prepare the uterus for pregnancy. The uterus can be affected by various disorders, including uterine fibroids (noncancerous growth), endometriosis (when the tissue that normally lines the uterus grows outside of it), and uterine prolapse (the descent or displacement of the uterus into the vaginal canal).

The fallopian tubes also known as the uterine tubes or the oviducts, are slender, tubular-like structures that extend from each side of the uterus. They have a funnel- shaped opening called the infundibulum; which is surrounded by fingerlike projections called fimbriae. The primary function of the fallopian tubes is to transplant the released egg (ovum) from the ovary to the uterus. Fertilization of the egg by sperm usually occurs within the fallopian tubes. The tubes also provide a suitable environment for early embryonic development. The fallopian tubes are influenced by hormonal changes in the female body. During ovulation, hormonal signals cause the fimbriae to sweep over the ovary, ensuring that the released egg enters the fallopian tube. A disorder of the fallopian tube includes blockages or obstruction that prevents the eggs from reaching the uterus, which can lead to infertility or ectopic pregnancy (when the fertilized egg implants outside the uterus). The present study aimed to evaluate the effect of graded doses of cloves on the uterus and fallopian tube histology. Therefore, the findings from this study can serve as a foundation for future studies to explore the underlying mechanisms by which cloves exert effects on the female reproductive system. Ultimately the results of this study may contribute to the development of evidence-based guidelines for safe and effective use of cloves in relation to women's reproductive health.

MATERIALS AND METHODS

Collection and identification of plant material

Syzgium aromatcum (Clove) was bought from Swali market, Bayelsa state, Nigeria in February, 2024. The plant material was identified at the Forest Research Institute of Nigeria, Ibadan, Nigeria. An herbarium specimen was deposited at the hebarium unit of the institute with voucher number FHI: 347261.

Preparation of extract

The powdered clove (5 g) was mixed with 20 mL of water and then placed on a shaker at a speed of 1000 rpm and kept overnight. The mixture was then filtered through a Whatman filter paper and centrifuged at 2000 rpm for 5 min. The supernatant was transferred into sterile test tube and stored in the refrigerator at 4°C.

Experimental animals and grouping

Twenty (20) Wistar rats weighing between 160 and220 g were bought from the animal house of the University of Port Harcourt and kept in a well-ventilated environment and were feed with normal rat feed and drinking water for fourteen days for acclimatization before the start of the experiment.

After two weeks of acclimatization, the rats were weighed and randomly divided into four (4) groups (I - IV) of five animals per group. Group I serves as the control group, and received no extract but normal rodent fed and saline, while Groups II, III and IV received graded doses of the extract (2 mL, 4 mL, and 6 mL, respectively) once daily for a period of 30 days by oral administration.

Collection of organs for histological analysis

At the end of the experimental period, the animals were fasted for 12 hours and thereafter sacrificed. The uterus and fallopian tubes were harvested for histological analysis using (H&E) (X400).

Ethical approval

Ethical approval was obtained from the board of the Department of Human Physiology, Bayelsa Medical University, Yenagoa, Bayelsa State, with reference number BMU-AREC/APP/05/011/02. The experiment was performed in accordance with NIH protocol for the use of laboratory animals.

RESULT AND DISCUSSION

In the present study, the effect of graded doses of *Syzygium aromaticum* (clove) extract on uterine and fallopian tube tissues were investigated in Wistar rats. Histological analysis of the uterus and fallopian tubes of healthy untreated rats (control) showed normal uterine features with intact luminal epithelium, endometrial glands, and stroma, as well as normal fallopian tube features, with intact blood vessels, mucosal folds, and lumen. Treatment with low and moderate doses (2 mL and 4 mL, respectively) of clove extract did not alter the uterine or fallopian tube tissue architecture as the histological examination of these tissues in rats in groups II and III displayed features characteristics of normal uterus and fallopian tubes, with intact endometrial glands, well-oriented stroma, epithelium, myometrium, and glands (uterus), as well as normal mucosal folds and lumen (fallopian tube).. However, treatment with high dose (6 mL) of clove extract resulted in mild degeneration of epithelial, and mucosal cells, vacuolizations and apoptotic cells were also observed in the uterus and fallopian tubes, indicating potential toxic effect on the uterus and fallopian tubes. The details of these observations are presented as follows; Figure 1 displayed the photomicrograph of uterine tissue of female Wistar rats in the control group, revealing normal uterine tissue with well oriented uterine cavity (UC) and intact luminal columnar epithelium (ILCE). There were also intact normal endometrial glands (NEG) and endometrial stroma (ES). Figure 2 shows the photomicrograph of a representative uterine tissue of female Wistar rats treated with low dose (2 mL) of *Syzygium aromaticum* extract (Group 2).

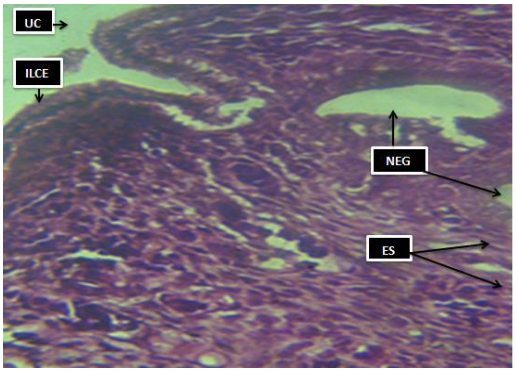

Figure 1: Photomicrograph of uterine tissue of Wistar rat in Group I (Control Group) (H & E) (X400). Uterine cavity (UC), Intact luminal columnar epithelium (ILCE), Normal Endometrial Glands (NEG), Endometrial stroma (ES)

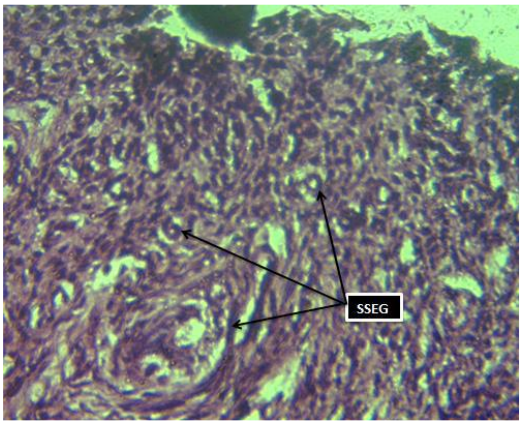

Figure 2: Photomicrograph of uterine tissue of Wistar rat in Group II [treated with low dose (2 mL) of *Syzygium aromaticum* extract] (H & E) (X400). Short, straight and elongated endometrial glands (SSEG)

The photomicrograph revealed normal tissue architecture, with intact short, straight and elongated endometrial glands (SSEG). Figure 3 presents the photomicrograph of uterine tissue of female Wistar rats treated with moderate dose (4 mL) of *Syzygium aromaticum* extract (Group 3). The photomicrograph displayed normal uterine histology with well oriented endometrial stroma (ES), epithelium (E), myometrium (M) and endometrial glands (EG). The features as shown in Figures 1 - 3 are indicative of a possible efficient regulatory roles of estrogen and progesterone that

would have been responsible for controlled tissue proliferation, remodeling, and breakdown during estrous cycle in the study animal models.

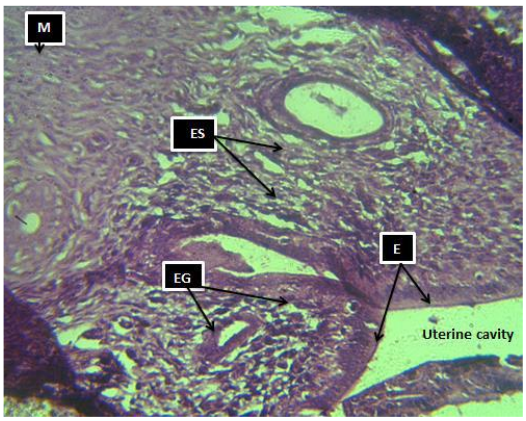

Figure 3: Photomicrograph of uterine tissue of Wistar rat in Group III [treated with moderate dose (4 mL) of *Syzygium aromaticum* extract] (H & E) (X400). Myometrium (M), Endometrial Stroma (ES), Epithelium (E), Endometrial Glands (EG)

On the other hand, the photomicrograph of representative uterine tissue of female Wistar rats treated with high dose (6 mL) of *Syzygium aromaticum* extract (Group 4) revealed mild vacuolations (VL), apoptotic cells (AC) and mildly degenerative epithelial cells (MDEC) (Figure 4). Such features may slightly distort the basic functions of the uterine tissues in the study group.

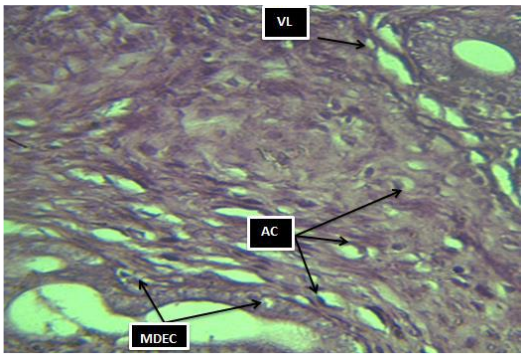

Figure 4: Photomicrograph of uterine tissue of Wistar rat in Group IV [treated with high dose (6 mL) of *Syzygium aromaticum* extract] (H & E) (X400). Vacuolations (VL), Apoptotic cells (AC), Mildly degenerative epithelial cells (MDEC)

In the same vein, the photomicrograph of fallopian tube of female Wistar rats in the control group as presented in Figure 5 revealed intact blood vessels (IBV), mucosal folds (MF) and lumen (L).

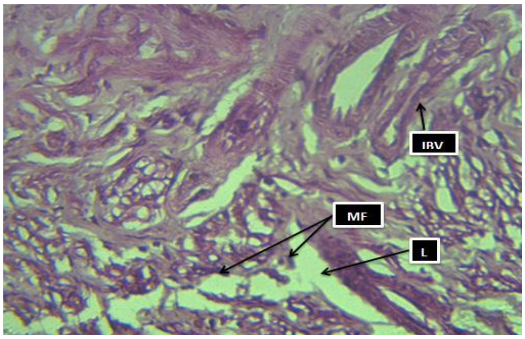

Figure 5: Photomicrograph of fallopian tube tissue of Wistar rat in Group I (Control Group) (H&E) (X400), Intact Blood vessel (IBV), Mucosal folds (MF), Lumen (L)

Similarly, the photomicrograph of fallopian tube of female Wistar rats treated with low dose of *Syzygium aromaticum* extract (Group 2) was seen to be normal showing normal mucosal folds (MF), lumen (L), mucosa (IM) and muscularis layer (Figure 6).

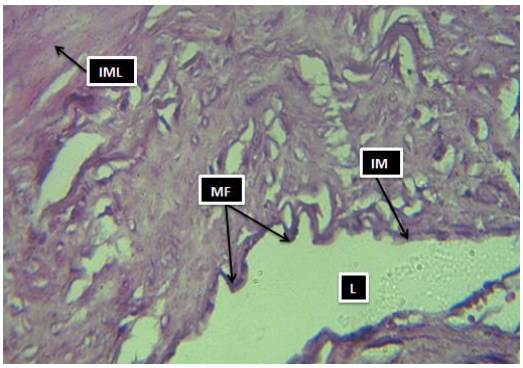

Figure 6: Photomicrograph of fallopian tube tissue of Wistar rat in Group II [treated with low dose (2 mL) of *Syzygium aromaticum* extract] (H & E) (X400). Mucosal folds (MF), Lumen (L), Intact Mucosa (IM), Intact Muscularis layer (IML)

For the rats treated with moderate dose (4 mL) of *Syzygium aromaticum* extract (Group 3), the fallopian tube appeared normal, with ciliated mucosa cells (CCM) layer and folds with intact lumens (L) (Figure 7). Finally, histological analysis of the fallopian tube of rats treated with high dose (6 mL) of *Syzygium aromaticum* extract (Group 4) revealed mildly degenerated mucosa (MDM), vacuolization (VL) and apoptotic cells (AC) (Figure 8). These findings suggest that *Syzygium aromaticum* extract may have dose-dependent effects on female reproductive tissues in rats.

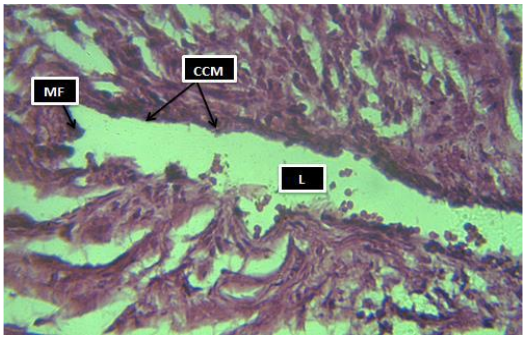

Figure 7: Photomicrograph of fallopian tube tissue of Wistar rat in Group III [treated with moderate dose (4 mL) of *Syzygium aromaticum* extract] (H & E) (X400). Lumen (L), Ciliated cells of mucosa (CCM), Mucosal folds (MF)

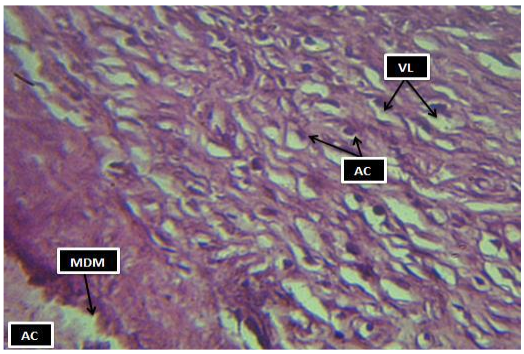

Figure 8: Photomicrograph of fallopian tube tissue of Wistar rat in Group IV [treated with high dose (6 mL) of *Syzygium aromaticum* extract] (H & E) (X400). Vacuolization (VL), Apoptotic cells (AC), Mildly degenerated mucosa (MDM), Lumen (L)

Overall, the findings from this study are consistent with the findings from previous studies, where *Syzygium aromaticum* extract were shown to exert varying degrees of effects on the female reproductive tissues, including the uterus and the fallopian tubes, in a dose-dependent manner.[15-17] Low and moderate doses appeared to maintain normal tissue structures, while high doses resulted in mild degenerative changes.

CONCLUSION

The findings from the present study suggest that *Syzygium aromaticum* extract may have dose-dependent effects on female reproductive tissues, particularly the uterus and the fallopian tubes. Low and moderate doses may maintain normal tissue architecture, while high doses may result in mild degenerative changes

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHORS DECLARATION

The authors hereby declare that the works presented in this article are original and that any liability for claims relating to the content of this article will be borne by them.

ACKNOWLEDGMENT

The authors would like to thank Mrs. Precious Wadioni for her assistant in the procurement of reagents and laboratory consumables used for this study.

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