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Studies on the Effect of *Musa paradisiaca* on the Morphology and Microanatomy of Some Female Reproductive Organs of Animal Model

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ABSTRACT

Musa paradisiaca, a staple food abundant in Vitamins C and E, exhibits antioxidant properties and has been traditionally employed in managing reproductive health concerns. This study aimed to evaluate the impact of *Musa paradisiaca* aqueous extract on body weight and ovarian histomorphology in Wistar rats. Thirty adult female Wistar rats (100-150 g) were randomly divided into three groups (n=10). Group I received standard rat feed and water, Group II received a low dose of *Musa paradisiaca* (200 mg/kg BW), and Group III received a high dose of *Musa paradisiaca* (400 mg/kg BW). Extracts were administered daily via oral gavage for 21 days. Twenty-four hours after the last dose, animals were sacrificed, and the ovaries and fallopian tubes were harvested for histomorphological analysis. The results reveal a significant increase in body weight of the treated animals. Histomorphological observations showed positive effects on ovarian tissue, especially in the treated groups, revealing an improved tunica albuginea layer, increased developing follicles, and enhanced follicular and granulosa cellular architecture, while the fallopian tube showed slightly branched tubal mucosal folds, moderate and thickened epithelial layers with remarkable epithelial cell hyperplasia and condensed connective tissue stoma.
This study suggests that *Musa paradisiaca* may improve ovarian and fallopian cellular activities, improving female rats' overall reproductive health.

Keywords: *Musa paradisiaca*, Ovary, Follicular cells, Wistar rat.

Introduction

Infertility is a global health issue affecting millions of individuals and couples worldwide. According to the World Health Organization (WHO), infertility is defined as the inability to conceive after 12 months or more of regular, unprotected sexual intercourse.[1] Infertility can stem from various factors, including physiological, psychological, and environmental causes, with both male and female counterparts contributing equally to the problem.[1] Several studies have highlighted the increased prevalence of infertility in recent times. A systematic analysis estimated that 48.5 million couples experienced infertility in 2020, with a global age-standardised prevalence of 1,571 per 100,000 couples.[1] This finding underscores the pressing need for improved prevention, diagnosis, and treatment strategies for infertility. Throughout history, medicinal plants have been employed for their therapeutic attributes, offering relief from the symptoms of various ailments. Deeply rooted in cultural traditions, these natural remedies present a valuable alternative to synthetic medicines developed in laboratory settings. The rich heritage of medicinal plant use in diverse cultural contexts underscores their longstanding importance in herbal medicine and their ongoing significance as sources of therapeutic benefit.[2]

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Illustrative examples of medicinal plants include ginger, green tea, and walnuts, which offer vital nutrition and possess therapeutic attributes that substantiate their application in conventional remedies. Given their status as rich sources of bioactive compounds, medicinal plants present promising avenues for advancing and creating novel therapeutic agents. Emphasising the significance of exploring and comprehending the vast potential of these natural resources, continued research on medicinal plants can unveil valuable insights into their therapeutic benefits, ultimately paving the way for innovative treatments addressing many health concerns.[3]

Musa paradisiaca (*Musa acuminata and Musa balbisiana*) is a sterile triploid that is considered in warm climates for its tasty yellow-skinned fruits (plantain). It is commonly called French plantain.[3-4] *Musa paradisiaca* (*Mus.Par.*) is a herbaceous plant characterised by a sturdy, tree-like pseudostem and a cluster of elongated, deep green, oval leaves with a distinct mid-rib. Each plant yields a single, drooping, spike-like inflorescence, which features sizable bracts that open progressively. These bracts are ovate, measuring 15-20 cm in length, and showcase a concave, dark red hue with a fresh appearance. The fruits produced by this plant are oblong, fresh, and measure 5-7 cm in length in their wild form, although they can grow longer in cultivated varieties. *M. paradisiaca* is a tree-like perennial herb that grows 5-9 m in height, with tuberous rhizome hard long pseudostem. The inflorescence is big with a reddish brown back and is eaten as vegetables. The ripe fruits are sweet and juicy, and the peel is thicker than other bananas.[5] The fruits of *M. paradisiaca* are locally used in diarrhoea (unripe), dysentery, intestinal lesions in ulcerative colitis, diabetes, uremia, nephritis, hypertension, and cardiac disease.[5] The flowers are used in dysentery and menorrhagia. The stem juice of the fruited plant is used for treating diarrhoea, dysentery, cholera, and menorrhagia. The roots are used for anthemic blood disorders and venereal diseases.[5-6]

The female ovaries exhibit a whitish hue and are situated in the ovarian fossa, a region adjacent to the uterus's lateral wall. This fossa is demarcated by the external iliac artery, the ureter, and the internal iliac

artery. A dense connective tissue capsule envelops the ovaries and comprises an outer cortex and an inner medulla.[7] The ovaries lie within the peritoneal cavity of either side of the uterus, to which they are attached via a fibrous cord called the ovarian ligament. The ovaries are uncovered in the peritoneal cavity but are tethered to the body wall via the broad ligament of the uterus. The part of the broad ligament of the uterus that covers the ovary is known as the mesovarium. The ovarian pedicle is made up of the fallopian tube, mesovarium, ovarium ligament, and ovarian blood vessels, and the surface of the ovaries is covered with a membrane consisting of a lining of simple cuboidal to columnar-shaped mesothelium called the germinal epithelium. The outer layer is the ovarian cortex, which consists of ovarian follicles and stroma between them.[8] Functionally, the ovaries are very important in the overall reproductive functions of the body. Many of the functions are directly controlled or indirectly by the ovaries. First is oogenesis, the process by which the female body produces eggs. This process occurs before the birth, and each female child is born with all the eggs she will need for her lifetime. Oogenesis is a form of meiosis or sex cell reproduction. Each egg will have 23 chromosomes, half the number required for humans to develop correctly. Likewise, a sperm cell has 23 chromosomes; when an egg and sperm unite, the total chromosome number is restored.[9]

Ovarian disease can be classified as an endocrine disorder or a disorder of the reproductive system. If the egg fails to release from the follicle in the ovary, an ovarian cyst may form. Some ovarian cysts are common in healthy women; some women have more follicles than usual, inhibiting the follicles from growing normally, and this will cause cycle irregularities. Some of these disorders include endometriosis, ovarian cysts, ovarian epithelial cancer, and ovarian germ cell tumour.[10] The fallopian or uterine tubes are essential for the female reproductive system. These slender, trumpet-shaped structures extend from the uterus to the ovaries, serving as the site of fertilisation and the pathway for egg transportation.[11] Anatomically, the fallopian tubes have four main parts: the infundibulum, ampulla, isthmus, and interstitial portion.[12] The infundibulum contains finger-like projections called fimbriae, which facilitate the capture of the released oocyte from the ovary. The ampulla is the widest and longest part, serving as the usual fertilisation site, while the isthmus and interstitial portion connect the tube to the uterine cavity.[13]
The fallopian tubes exhibit physiological changes during the menstrual cycle, promoting sperm transport, fertilisation, and early embryonic development.[14] Hormonal fluctuations regulate the function and motility of the ciliated and secretory cells lining the tubes, enabling proper oocyte transport and reproduction.[15] The fallopian tubes play a critical role in female fertility and reproduction. However, fallopian tubes can suffer from various pathologies, such as infections, inflammation, endometriosis, and tubal factor infertility.[16] Salpingitis, an inflammatory condition affecting the tubes, often arises due to sexually transmitted diseases and can lead to scarring, adhesions, and tubal occlusion.[14] Tubal ectopic pregnancy and malignancies may also occur, necessitating timely diagnosis and management.[17]
This research aims to evaluate the effect of *Musa Paradisiaca* on the morphology and microanatomy of some female reproductive organs in animal models using the H&E staining method and assess the body weights of the experimental animals.

Materials and Methods

Ethical Approval
Ethical approval for the experiment was obtained from the Faculty of Basic Medical Ethical Committee for the use of experimental animals, with an ethical certificate No. FBMS/2023/05/1005 issued. The guidelines for using animals in research were duly followed.

Materials
The apparatus and equipment used in this study include animal cages, feeding troughs, syringes/needles, dissecting set, EDTA bottles, sample bottles, sensitive weighing balance, desiccators, glass slides, compound light microscope, water bath, electronic weighing balance, and measuring cylinders. Chemicals and reagents used included xylene, Bouin's fluid, methylated spirit, formal saline, and normal saline.

Sample Collection
The plantain (*Musa Paradisiaca*) was obtained from the local market of Okuku in Yala Local Government Area of Cross River State in Nigeria. The unripe plantain was properly washed and peeled, sliced, and dried in an air-light room temperature of about 27℃ for 3 weeks, after which it was blended and kept in an air-tight container.

Extract Preparation
The plantain powder was soaked in a plastic container with table water (900 mL). The mixture was stirred perfectly and macerated for 24 hours before it was filtered with a cotton sieve. The filtrate was evaporated at 45℃ in a water bath to obtain a crude solid extract. The extract obtained was stored in a refrigerator until administration.

Experimental Animals
Thirty adult female Wistar rats were purchased from the animal house of the Department of Human Anatomy and Forensic Anthropology, University of Cross River State (UNICROSS) Okuku campus, and used for the study. The animals were kept in plastic cages under controlled light (12 hours daylight and 12 hours dark). They were fed with standard grower feed and water to administer the extract. They were handled according to the OECD 19 guidelines for the care of experimental animals.

Experimental Design
The experimental animals were randomly divided into 3 groups, each consisting of ten experimental animals.
Group A: This is the control group. The animals in this group were fed with food and water only.
Group B: The animals in this group were given food, water, and an extract of *Musa paradisiaca* at a low dose of 200 mg/kg Bw.
Group C: The animals in this group were given food, water, and an extract of *Musa paradisiaca* at a high dose of 400 mg/kg Bw.

Morphological Studies
The animals were weighed every 2 days throughout the experimental period (to record their body weights) using a sensitive weighing balance. This was usually done before the administration of the extract *Musa paradisiaca* to ascertain the morphological changes.

Termination of the Experiment
At the end of the administration of the extract, which lasted for 21 days, the animals in all three groups were sacrificed on the day following the final administration using cervical dislocation. The animal's ovaries were carefully removed and washed with 10% formalin.

Tissue Processing
The ovaries and fallopian of the animals were removed and preserved in a container in 10% buffer formalin; the organ was left for 72 hours to achieve good tissue penetration. The organ was placed on an ascending grade of ethanol for dehydration. Firstly, the organs were treated with 70% ethanol for an hour, followed by 95% ethanol, and lastly, with absolute alcohol for the same duration. The tissues were cleared on xylene for 15 minutes. Each of these was done 3 times. The tissue was impregnated in molten paraffin wax at 58℃ and allowed to stay overnight till the tissues formed blocks. The following morning, the tissue blocks were trimmed and sectioned at 3 to 5 µm thickness using a microtome. The achieved sections were mounted on albumenised glass slides.

Statistical Analysis
Statistical analysis was done using statistical package for social science (SPSS) version 16 Chicago Inc. One-way ANOVA. Bontewoni's multiple data comparison was used to perform the analysis result of

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descriptive statistics of experimental data presented as mean standard error (mean ± SEM). Paired sample T-tests were considered statistically significant at $p<0.05$.

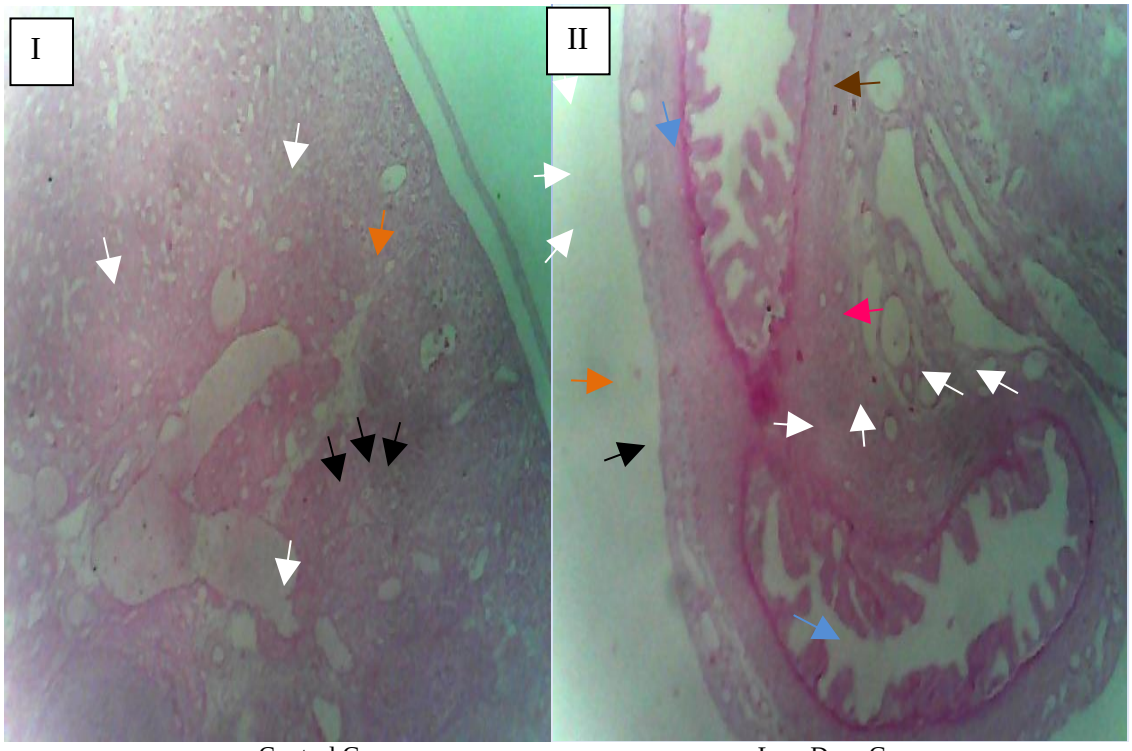
Results and Discussion

Results from the present study showed a statistically significant increase in the final body weights of rats in the treatment groups (low and high doses) compared to rats in the control group (Table 1). The ovaries of control group rats displayed regular features, including a typical tunica albuginea (brown arrows), stroma with normal connective tissue (black arrows), and primary follicles with unilaminar (single-layered) follicular cells (white arrows) Figure 1 (Plates I and III). In contrast, treated rats exhibited thicker tunica albuginea (brown arrows) and numerous primary follicles with multilaminar (multiple-layered) follicular cells (dark brown arrows) (Plates II and IV). Additionally, countless primordial follicles (PFCs) and stroma with condensed/saturated connective tissue (black arrows) were observed in the ovaries of low and high-dose group rats, respectively (Plates II and IV). In the fallopian tubes, control group rats showed typical tubal architecture with slightly branched tubal mucosal folds (brown arrows), moderate epithelial layer with normal epithelial cells (white arrows), and connective tissue stroma (black arrows) (Plates V and VII). However, rats in the low and high-dose groups displayed multiple branched tubal mucosal folds (brown arrows), moderate to thickened epithelial layers with moderate to remarkable epithelial cell hyperplasia (white arrows), and slightly to remarkably condensed connective tissue stroma (black arrows) (Plates VI and VIII).

Table 1: Showing Changes in Body Weights of Experimental Rats

Groups	Initial wt	Final wt
Control	91.40 ± 5.467	115.0 ± 3.310
Low Dose	133.8 ± 3.094	152.4 ± 6.723
High Dose	135.1 ± 6.125	160.2± 6.018

Values are presented as Mean ± SEM ($p<0.05$)



Control Group Low Dose Group

Figure 1 (I-II): Histomorphological analysis of ovarian and fallopian tube tissues in rats treated with *Musa paradisiaca* extract using Hematoxylin and Eosin Staining.

Plate I: Control Group: showing Normal Tunica Albuginea (Brown Arrow), Stroma having Normal Connective Tissue (Black Arrows), and Primary Follicles with Unilaminar (single-layered) Follicular Cells (White Arrows) H & E x100.

Plate II: Low Dose Group: showing Moderately Thick Tunica Albuginea (Brown Arrow), Stroma having Normal Connective Tissue (Black Arrow), Medullary Blood Vessels (Turquoise Blue Arrow), Numerous Primordial Follicles (White Arrows), Primary Follicle with Unilaminar (single-layered) Follicular Cells (Pink Arrow) and Primary Follicle with Multilaminar (multiple layered) Follicular Cells (Dark Brown Arrow) H & E x 100.

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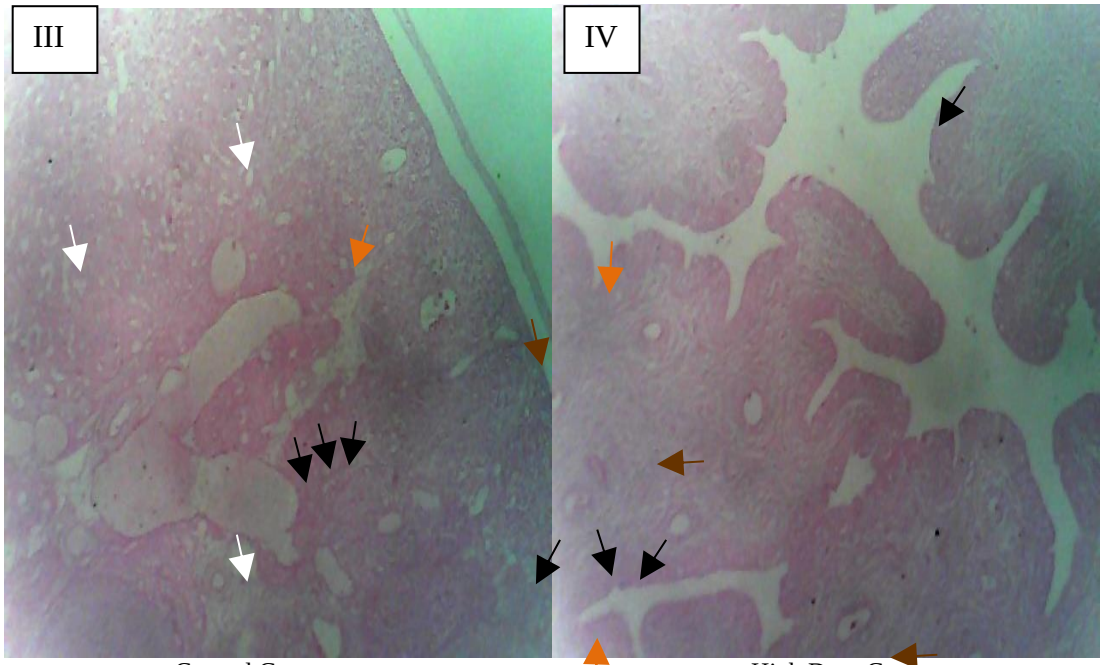

Control Group High Dose Group

Figure 1: (III-IV) Histomorphological analysis of ovarian and fallopian tube tissues in rats treated with *Musa paradisiaca* extract using Hematoxylin and Eosin Staining.

Plate III: Control Group: showing Normal Tunica Albuginea (Brown Arrow), Stroma having Normal Connective Tissue (Black Arrows), and Primary Follicles with Unilaminar (single-layered) Follicular Cells (White Arrows) H & E x100.

Plate IV: High Dose Group: showing Severely Thick Tunica Albuginea (Brown Arrows), Stroma with Condensed/saturated Connective Tissue (Black Arrows), and Numerous Primary Follicles with Multilaminar (multiple layered) Follicular Cells (Dark Brown Arrows) H & E x 100

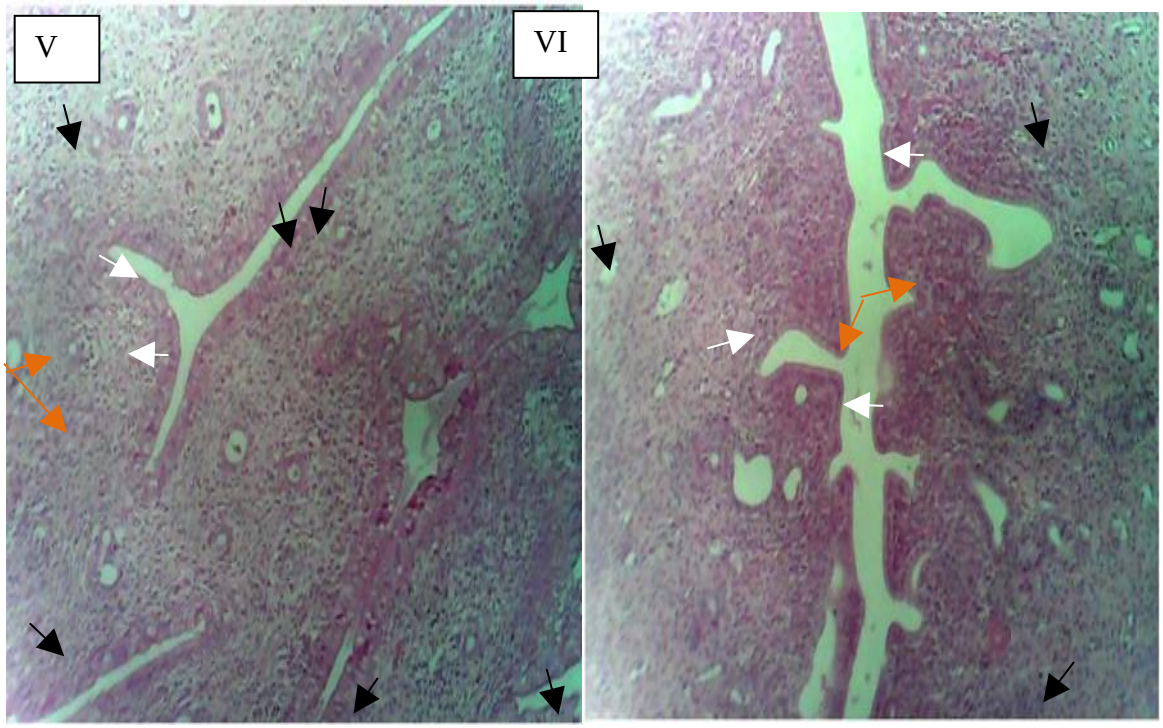

Figure 1: (V-VI) Histomorphological analysis of ovarian and fallopian tube tissues in rats treated with *Musa paradisiaca* extract using Hematoxylin and Eosin Staining.

Plate V: Control Group: showing Normal Tubal Architecture with Slightly Branched Tubal Mucosal Folds (Brown Arrows), Moderate Epithelial Layer with Normal Epithelial Cells (White Arrows), and Connective Tissue Stroma (Black Arrows) H & E x 100.

Plate VI: Low Dose Group: showing Tubal Architecture with Multiple Branched Tubal Mucosal Folds (Brown Arrows), Moderate Epithelial Layer with Moderate Epithelial Cell Hyperplasia (White Arrows) and Slightly Condensed Connective Tissue Stroma (Black Arrows) H & E x 100.

Morphological findings from this present study revealed an observable significant (p<0.05) increase in the final mean body weight compared to the previously observed initial body weight. The mean final body weight of rats in the low dose (152.4 ± 6.723) and high dose (160.2 ± 6.018) groups were significantly (p<0.05) higher than their initial body weights (133.8 ± 3.094) and (135.1 ± 6.125), respectively (Table 1) which agrees with the research of.[18] The experimental rats showed a 13.42% gain in weight after using *Mus. Par*. Extract. In this present study, histological observations revealed that *Mus. Par.* administration at a low dose caused a high proliferation of primordial and primary follicles with unilaminar (single-layered) follicular cells, thereby suggesting a positive effect of *Mus. Par*. on oogenesis. The tunica albuginea, a protective fibrous covering of the ovary, was moderately thick. This implies that extract at a low dose can play a vital role in the treatment of female sexual dysfunctions. Although less substantial work has been done on the effect of *Mus. Par.* on the histomorphology of rats ovaries. The observations from this present work aligned with the previous findings.[18-19] on the testis, reporting that *Mus. Par.* has reproductive enhancing potentials when consumed moderately and increases spermatogenesis in infertile diabetic patients, respectively. This effect was undoubtedly evident as an improvement in the quantity and quality of spermatozoa in treated adult Wistar rats, especially at low doses. At high doses, *Mus. Par*. administration caused stromal connective tissue condensation and saturation with severe thickening of the tunica albuginea. Excessive thickening of ovarian tunica albuginea and cortical stroma have been indicated as features of women with polycystic ovarian syndrome (PCOS), and this is associated with ovulation pain in PCOS patients.[20] It is associated with infertility, menstrual dysfunction, and hyperandrogenism.[21] Soft tissue fibrosis is marked by excessive connective tissue deposition.[22] Fibrosis or excess accumulation of extracellular matrix can disrupt tissue architecture and function.[23] Fibrosis is characterised by excessive extracellular matrix accumulation, usually as a result of excess synthesis and deposition of collagen. It has been implicated in many connective tissue diseases.[24] This can also be due to the hyperactivity of fibroblasts.[25] Uncontrolled or chronic condensation of connective tissue fibres can decrease organ function, leading to organ dysfunction, failure, and death.[20] Uncontrolled inflammatory processes can also lead to fibrosis.[22] Ovarian fibrosis is a pathological condition primarily associated with ageing and can lead to ovarian dysfunction. Tissue fibrosis plays a crucial role in tumorigenesis and is a risk factor for ovarian cancer.[15] The presence of collagen condensation/saturation observed in the ovaries of rats administered with a high dose of *Musa paradisiaca* in this study indicates that consuming this plant in large quantities could predispose female individuals to age-related ovarian histomorphological changes, such as fibrosis and tumour development. These changes may increase the risk of ovarian dysfunction and, consequently, lead to infertility.[26] Furthermore, more primary follicles with multilaminar (multiple-layered) follicular cells were observed, suggesting an enhancement of the follicle maturation process promoting ovulation. This finding implies that administering high doses of Musa paradisiaca can stimulate ovulation in females.[26] While the study conducted by[26] focused on the protective effects of *Musa paradisiaca* on reproductive organs, the findings from the current study provide insights into the potential risks associated with high-dose consumption of this plant. Similarly, this study revealed significant histomorphological changes in the fallopian tubes of Wistar rats administered *Musa paradisiaca* aqueous extract at different doses. The observed alterations in the treated groups, particularly regarding the tubal architecture, epithelial layer thickness, and connective tissue stroma, necessitate further analysis and interpretation. The increased branching in the tubal mucosal folds of the treated groups could suggest a stimulatory effect of *Musa paradisiaca* extract on the growth and proliferation of tubal epithelial cells. Previous studies have indicated that plant extracts containing phytoestrogens can induce morphological changes in reproductive tissues.[27] Given that *Musa paradisiaca* is rich in phytochemicals, including flavonoids and phenols[28], the potential hormonal effects of these compounds might explain the observed alterations in the fallopian tubes. The moderate to remarkable epithelial cell hyperplasia and thickening of the epithelial layer in the treated groups might be attributed to the mitogenic and proliferative effects of the plant extract. A study reported that certain plant-derived compounds, such as saponins, could stimulate cell growth and proliferation.[27] *Musa paradisiaca* also contains saponins[29], contributing to the increased epithelial thickness in the fallopian tubes. Also, the observed condensation of connective tissue stroma in the treated groups could indicate increased collagen deposition and extracellular matrix remodelling. Studies have suggested that some plant-derived compounds can modulate the activity of fibroblasts and myofibroblasts, promoting collagen synthesis and extracellular matrix reorganisation.[30] This might be a plausible explanation for the changes in connective tissue stroma observed in this study.

Conclusion

The extract positively impacted the ovary, especially when consumed in small and moderate quantities. The revealed positive effects include the proliferation of developing follicles, enhancement of follicular and granulosa cellular activities, promotion of good ovarian histomorphology and cytoarchitecture, and improved female reproductive health. It should be noted that consumption of the extract in high or uncontrolled quantities can have adverse effects on histomorphology of the ovary and as well as female reproductive health, thereby predisposing consumers to organ ageing changes and precancerous conditions, including fibrosis, which can result in organ dysfunction and infertility.

Conflict of Interest

The authors declare no conflict of interest.

Authors' Declaration

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

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