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Protective Effects of Graded Doses of Aqueous Seed Extract of *Dennettia tripetala* on Ovarian Biochemical, Hormonal, and Microbiological Alterations in Bisphenol A-Induced Oxidative Stress in Female Wistar Rats

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ABSTRACT

Background: Bisphenol A (BPA) is an endocrine-disrupting chemical associated with oxidative stress and ovarian dysfunction. *Dennettia tripetala* is a medicinal plant with reported antioxidant and antimicrobial properties.

Aim: This study evaluated the protective effects of graded doses of aqueous seed extract of *Dennettia tripetala* on ovarian biochemical, hormonal, and microbiological alterations in bisphenol A-induced oxidative stress in female Wistar Rats.

Materials and Methods: Thirty-five (35) adult female Wistar rats were randomly assigned into seven groups (n = 5). Group I served as the normal control, Group II received BPA only, Group III received BPA and Vitamin C, while Groups IV–VII received BPA and aqueous seed extract of D. tripetala at 100, 200, 400, and 800 mg/kg body weight, respectively, for 28 days. Phytochemical, biochemical, hormonal, microbiological, and histopathological analyses were performed using standard methods.

Results: Phytochemical screening revealed the presence of flavonoids, phenolic compounds, alkaloids, tannins, saponins, terpenoids, glycosides, and steroids, with flavonoids and phenolic compounds being the most abundant. BPA exposure significantly increased ovarian malondialdehyde levels and microbial burden while reducing antioxidant parameters and reproductive hormone concentrations. Histopathological examination also revealed marked ovarian damage. Treatment with aqueous seed extract of D. tripetala significantly and dose-dependently reduced oxidative stress, restored estradiol, progesterone, follicle-stimulating hormone, and luteinizing hormone concentrations, decreased microbial counts and isolates, and improved ovarian histoarchitecture. The 800 mg/kg dose produced effects comparable to Vitamin C.

Conclusion: Aqueous seed extract of *D. tripetala* demonstrated significant ovarian protective activity against BPA-induced toxicity, highlighting its potential as a natural therapeutic agent for oxidative stress-related reproductive disorders.

Keywords: *Dennettia tripetala*; phytochemical; Bisphenol A; oxidative stress; ovary; reproductive hormones; antioxidant activity; ovarian microbiology; histopathology; female reproductive health.

1. Introduction

For centuries, medicinal plants have been recognized as important reservoirs of biologically active compounds and remain integral to healthcare, pharmaceutical development, and the prevention and treatment of numerous diseases [1-3]. Their medicinal efficacy is primarily linked to the presence of diverse phytoconstituents, including flavonoids, alkaloids, tannins, saponins, terpenoids, and phenolic substances [4-6]. These compounds possess a wide range of pharmacological properties, notably antioxidant [7], anti-inflammatory [8], antimicrobial [7], and hormone-regulating effects [9].

Through their interactions with various tissues and physiological pathways, these phytochemicals contribute to the maintenance of cellular integrity and normal organ function [10-13]. Within the reproductive system, they have been reported to support hormonal balance, mitigate oxidative damage, and enhance reproductive tissue health [14-16]. As a result, growing scientific interest has focused on the use of medicinal plants as natural therapeutic agents for managing reproductive dysfunctions linked to oxidative stress and related pathological conditions [17-19].

The maintenance of female reproductive competence is critically dependent on the normal architecture and physiological activity of the ovaries [20]. As the primary reproductive organs, the ovaries coordinate essential processes such as follicular growth, oocyte development, and the biosynthesis of steroid hormones, particularly estrogen and progesterone, which regulate reproductive cyclicity and fertility [21, 22]. Any disturbance in ovarian cellular equilibrium may adversely affect these functions and ultimately compromise reproductive performance [23].

Among the factors capable of disrupting ovarian physiology, oxidative stress has received considerable attention due to its detrimental effects on cellular metabolism and tissue integrity. Excessive generation of reactive oxygen species can overwhelm endogenous antioxidant defenses, resulting in cellular damage that interferes with follicular maturation and hormone production [24, 25]. Such alterations may impair steroidogenic pathways, reduce oocyte quality, and contribute to subfertility or infertility [26]. Consequently, the preservation of redox balance within ovarian tissues is recognized as a fundamental requirement for optimal reproductive health [27].

Beyond oxidative injury, growing evidence suggests that disturbances in the microbial ecosystem of the female reproductive tract, often accompanied by inflammatory responses, play significant roles in the pathogenesis of various gynecological disorders [28-30]. Dysbiosis may promote tissue damage, alter local immune regulation, and create conditions that adversely affect reproductive function [31].

Among the environmental contaminants that threaten female reproductive health, Bisphenol A (BPA) has emerged as a major endocrine-disrupting chemical due to its widespread use in the manufacture of polycarbonate plastics and epoxy resins [32]. Human exposure occurs primarily through contaminated food and beverages, leading to the accumulation of BPA in biological tissues [32,33]. Numerous studies have shown that BPA induces excessive generation of reactive oxygen species, promotes lipid peroxidation, disrupts antioxidant defense mechanisms, alters reproductive hormone secretion, and causes structural damage to ovarian tissues. These toxic effects have been associated with impaired follicular development, reduced fertility, and other adverse reproductive outcomes [32-34].

While environmental toxicants such as Bisphenol A pose significant risks to reproductive health, increasing attention has been directed toward plant-derived compounds as potential protective agents against oxidative and endocrine-mediated tissue damage. Among such plants is *Dennettia tripetala* (pepperfruit), a member of the Annonaceae family that is extensively consumed across West Africa as both a dietary component and a traditional medicinal resource. The seeds of the plant contain a diverse array of bioactive phytochemicals, including flavonoids, alkaloids, tannins, saponins, and volatile oils, which have been associated with numerous biological and therapeutic effects [35,36].

Despite the growing body of evidence supporting the medicinal value of *D. tripetala*, information concerning its effectiveness in preventing or ameliorating BPA-induced ovarian injury remains limited. Existing studies have largely focused on its general pharmacological properties, with relatively few investigations providing an integrated assessment of ovarian biochemical markers, reproductive endocrine function, microbial status, and histopathological changes following treatment with graded doses of its aqueous seed extract. The paucity of such

comprehensive data restricts a thorough understanding of the mechanisms through which the plant may exert protective effects on female reproductive organs under conditions of chemically induced oxidative stress.

To address this gap, the present study evaluated the capacity of graded doses of aqueous seed extract of *D. tripetala* to mitigate ovarian dysfunction induced by Bisphenol A in female Wistar rats. Particular emphasis was placed on assessing changes in biochemical indicators of oxidative stress, reproductive hormone concentrations, microbiological parameters, and histological characteristics of ovarian tissues in order to determine the potential protective role of the extract against BPA-mediated reproductive toxicity.

1.1 Objectives of the Study

The aim of this study is to evaluate the protective effects of graded doses of aqueous seed extract of *Dennettia tripetala* on ovarian biochemical, hormonal, and microbiological alterations in bisphenol A-induced oxidative stress in female Wistar Rats. However, the objectives of the study are to:

1) Determine the phytochemical constituents of the aqueous seed extracts of *Dennettia tripetala***.**

2) Ascertain the effect of aqueous seed extract of D. tripetala on selected ovarian biochemical parameters (malondialdehyde (MDA), reduced glutathione (GSH), superoxide dismutase (SOD), catalase (CAT), and total proteinin) in Bisphenol A-induced oxidative stress.

3) Determine the effect of aqueous seed extract of D. tripetala on selected hormonal changes (malondialdehyde (MDA), reduced glutathione (GSH), superoxide dismutase (SOD), catalase (CAT), and total proteinin) in Bisphenol A-induced oxidative stress.

4) Establish the effect of aqueous seed extract of D. tripetala on selected serum reproductive hormones in Bisphenol A-induced oxidative stress.

5) Ascertain the microbial isolates recovered from the ovarian tissues of female Wistar rats exposed to Bisphenol A (BPA) and treated with Vitamin C or aqueous seed extract of D. tripetala at different doses l.

6) Validate the study by examining the histopathological features of ovarian tissues from female Wistar rats exposed to Bisphenol A (BPA) and treated with Vitamin C or aqueous seed extract of *D. tripetala* at different doses.

2. Materials and Methods

2.1. Materials

Fresh fruits of *D. tripetala* were used for the preparation of the aqueous seed extract. Bisphenol A (BPA), distilled water, phosphate-buffered saline (PBS), Whatman No. 1 filter paper, nutrient agar, MacConkey agar, blood agar, Sabouraud dextrose agar, normal saline, and analytical-grade chemicals were utilized for the study. Commercial ELISA kits for estradiol, progesterone, follicle-stimulating hormone (FSH), and luteinizing hormone (LH), as well as assay kits for malondialdehyde (MDA), reduced glutathione (GSH), superoxide dismutase (SOD), catalase (CAT), and total protein were employed. Standard laboratory equipment, including an analytical balance, homogenizer, centrifuge, spectrophotometer, ELISA microplate reader, incubator, oral gavage tubes, water bath, micropipettes, and glassware, were also used.

2.2. Methods

- **Collection and Authentication of Plant Material**

Fresh fruits of Dennettia tripetala were procured from Mile One Market, Port Harcourt, Rivers State, Nigeria. The plant material was taxonomically identified and authenticated by Prof. J.A. Onwugbuta-Enyi of the Plant Science Unit, Department of Biology, Faculty of Natural and Applied Sciences, Ignatius Ajuru University of Education, Rumuolumeni, Port Harcourt, Rivers State, Nigeria. A voucher specimen was subsequently prepared and deposited in the departmental herbarium for future reference and verification under Voucher Number IAUE/FNAS/BIO/PLS/2026/0066. The fruits of *D. tripetala* used in this study are shown in Figure 1.

Figure 1. *Dennettia tripetala* (pepper fruit).

Source: Adapted from The Guardian Nigeria (accessed June 2026).
https://guardian.ng/features/how-pepper-fruit-others-stop-prostate-cancer/

- **Preparation of Aqueous Seed Extract**

The fruits were washed thoroughly with distilled water, and the seeds were manually separated from the pulp. The seeds were air-dried at room temperature for two weeks and ground into a fine powder using an electric grinder. Five hundred grams (500 g) of the powdered sample was soaked in 2.5 L of distilled water for 48 h with intermittent stirring. The mixture was filtered through Whatman No. 1 filter paper, and the filtrate was concentrated in a water bath maintained at 45°C. The concentrated extract was stored in airtight containers at 4°C until use.

- **Phytochemical Screening**

Preliminary qualitative phytochemical screening of the aqueous seed extract of *Dennettia tripetala* was carried out to determine the presence of major bioactive constituents using standard methods described by Okari et al. [4]. The extract was screened for alkaloids, flavonoids, tannins, saponins, phenolic compounds, terpenoids, glycosides, and steroids.

- **Experimental Animals**

Thirty-five (35) adult female Wistar rats weighing between 150 and 200 g were used for the study and randomly assigned into seven experimental groups (n = 5).

- **Induction of Oxidative Stress**

Oxidative stress was induced in the experimental animals using Bisphenol A (BPA). Bisphenol A was dissolved in distilled water and administered orally at a dose of 50 mg/kg body weight once daily for 28 consecutive days. The selected dose was based on previous studies that demonstrated its ability to induce oxidative stress, endocrine disruption, and reproductive toxicity in experimental animals.

- **Experimental Grouping and Treatment**

Thirty-five adult female Wistar rats were randomly assigned into seven groups of five animals each:

Group I (Normal Control): Received distilled water only.

Group II (Negative Control): Received Bisphenol A (50 mg/kg body weight) only.

Group III (Positive Control): Received Bisphenol A (50 mg/kg body weight) and Vitamin C (100 mg/kg body weight).

Group IV (BPA + DT100): Received Bisphenol A (50 mg/kg body weight) and 100 mg/kg body weight of aqueous seed extract of *Dennettia tripetala*.

Group V (BPA + DT200): Received Bisphenol A (50 mg/kg body weight) and 200 mg/kg body weight of aqueous seed extract of *Dennettia tripetala*.

Group VI (BPA + DT400): Received Bisphenol A (50 mg/kg body weight) and 400 mg/kg body weight of aqueous seed extract of *Dennettia tripetala*.

Group VII (BPA + DT800): Received Bisphenol A (50 mg/kg body weight) and 800 mg/kg body weight of aqueous seed extract of *Dennettia tripetala*.

Bisphenol A was administered orally once daily for 28 consecutive days to induce oxidative stress. Vitamin C and the aqueous seed extract of *Dennettia tripetala* were administered orally by gavage one hour after BPA administration throughout the treatment period.

- **Sample Collection**

At the end of the treatment period, the animals were fasted overnight and euthanized under appropriate anesthesia. Blood samples were collected by cardiac puncture into plain tubes for serum preparation. The ovaries were aseptically excised, rinsed with cold physiological saline, blotted dry, and weighed. One ovary was processed for biochemical analysis, while the other was used for microbiological investigations.

- **Preparation of Ovarian Tissue Homogenates**

The ovarian tissues were homogenized in ice-cold phosphate-buffered saline (0.1 M, pH 7.4) to obtain a 10% (w/v) homogenate. The homogenates were centrifuged at 5,000 rpm for 15 min at 4°C, and the resulting supernatants were collected and stored at −20°C until biochemical analyses.

- **Determination of Ovarian Biochemical Parameters**

Ovarian tissue homogenates were analyzed for malondialdehyde (MDA), reduced glutathione (GSH), superoxide dismutase (SOD), catalase (CAT), and total protein using standard spectrophotometric procedures and commercially available assay kits according to the manufacturers' instructions.

- **Hormonal Analysis**

Serum concentrations of estradiol, progesterone, follicle-stimulating hormone (FSH), and luteinizing hormone (LH) were determined using enzyme-linked immunosorbent assay (ELISA) kits following the manufacturers' protocols.

- **Ovarian Microbiological Analysis**

Ovarian tissues were aseptically homogenized in sterile normal saline, serially diluted, and inoculated onto nutrient agar, MacConkey agar, blood agar, and Sabouraud dextrose agar. The inoculated plates were incubated under appropriate conditions, after which colony-forming units were enumerated. Representative colonies were identified using colony morphology, Gram staining, and standard biochemical tests.

- **Histopathological Evaluation of the Ovary**

Following sacrifice, ovarian tissues were carefully excised and immediately fixed in 10% neutral buffered formalin for 48 hours. The fixed tissues were processed by routine paraffin embedding techniques, dehydrated in ascending grades of ethanol, cleared in xylene, and embedded in paraffin wax. Tissue blocks were sectioned at 5 µm thickness using a rotary microtome, mounted on glass slides, and stained with hematoxylin and eosin (H&E). The stained sections were examined under a light microscope by a qualified histopathologist for evidence of morphological alterations, including follicular architecture, stromal integrity, vascular congestion, inflammatory cell infiltration, and degenerative changes. Representative photomicrographs were captured at appropriate magnifications.

- **Statistical Analysis**

Data generated from the study were expressed as mean ± standard deviation (SD). Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 25.0. Differences among groups were analyzed using one-way analysis of variance (ANOVA), followed by Tukey's post hoc multiple comparison test. Statistical significance was set at $p < 0.05$.

3. Results

3.1 Phytochemical Composition of Aqueous Seed Extract of Dennettia tripetala

Table 3.1 shows the qualitative phytochemical constituents of the aqueous seed extract of *D. tripetala*. The phytochemical screening revealed the presence of flavonoids, phenolic compounds, alkaloids, tannins, saponins, terpenoids, glycosides, and steroids in varying proportions. Flavonoids and phenolic compounds were highly abundant, while alkaloids, tannins, saponins, and terpenoids were moderately present. Glycosides and steroids were detected in lower amounts. These findings indicate that the aqueous seed extract contains diverse bioactive compounds that may contribute to its biological and pharmacological activities.

Table 3.1. Qualitative Phytochemical Screening of Aqueous Seed Extract of *D. Tripetala.*

Phytochemical Constituent	Result
Alkaloids	++
Flavonoids	+++
Tannins	++
Saponins	++
Phenolic compounds	+++
Terpenoids	++
Glycosides	+
Steroids	+

Key: + = Slightly present; ++ = Moderately present; +++ = Highly present; − = Absent.

3.2. Effect of Aqueous Seed Extract of *D. tripetala* on Ovarian Biochemical Parameters in Bisphenol A-Induced Oxidative Stress

Table 3.2 shows the ovarian biochemical parameters of female Wistar rats exposed to Bisphenol A (BPA) and treated with Vitamin C or graded doses of aqueous seed extract of *D. tripetala*. BPA exposure significantly increased ovarian MDA concentration and significantly decreased GSH, SOD, CAT, and total protein levels compared with the normal control group ($p < 0.05$). Treatment with Vitamin C and aqueous seed extract of *D. tripetala* significantly ameliorated these changes. The extract produced a dose-dependent reduction in MDA levels and corresponding increases in GSH, SOD, CAT, and total protein concentrations. The 800 mg/kg dose yielded values that were comparable to those observed in the Vitamin C-treated group.

Table 3.2. Ovarian biochemical parameters of female Wistar rats exposed to Bisphenol A and treated with aqueous seed extract of *D. tripetala* (Mean ± SD, n = 5).

Parameter	Normal Control	BPA Control	Vitamin C	DT100	DT200	DT400	DT800
MDA (nmol/mg protein)	3.62 ± 0.18^{e}	8.94 ± 0.41^{a}	4.35 ± 0.22^{d}	6.82 ± 0.34^{b}	5.96 ± 0.28^{c}	4.83 ± 0.23^{d}	3.98 ± 0.19^{e}
GSH (µmol/mg protein)	28.41 ± 1.32^{a}	15.23 ± 0.84^{e}	25.84 ± 1.18^{b}	18.72 ± 0.95^{d}	21.44 ± 1.06^{c}	24.67 ± 1.13^{b}	27.38 ± 1.24^{a}
SOD (U/mg protein)	16.24 ± 0.78^{a}	7.84 ± 0.41^{e}	14.82 ± 0.72^{b}	10.12 ± 0.51^{d}	11.96 ± 0.58^{c}	13.88 ± 0.65^{b}	15.76 ± 0.74^{a}

CAT (U/mg protein)	33.52 ± 1.65[a]	17.42 ± 1.03[e]	30.24 ± 1.48[b]	22.16 ± 1.21[d]	25.68 ± 1.34[c]	28.91 ± 1.42[b]	32.14 ± 1.56[a]
Total Protein (mg/mL)	5.98 ± 0.33[a]	3.82 ± 0.21[e]	5.64 ± 0.28[b]	4.41 ± 0.23[d]	4.92 ± 0.25[c]	5.38 ± 0.27[b]	5.81 ± 0.31[a]

Different superscripts within the same row indicate significant differences ($p < 0.05$).

3.3. Effect of Aqueous Seed Extract of *D. tripetala* on Serum Reproductive Hormones

Table 3.3 shows the serum reproductive hormone concentrations of female Wistar rats exposed to Bisphenol A (BPA) and treated with Vitamin C or aqueous seed extract of *D. tripetala* at doses of 100, 200, 400, and 800 mg/kg. BPA exposure significantly reduced serum estradiol, progesterone, follicle-stimulating hormone (FSH), and luteinizing hormone (LH) concentrations compared with the normal control group ($p < 0.05$). Treatment with Vitamin C and aqueous seed extract of D. tripetala significantly restored the concentrations of these reproductive hormones relative to the BPA control group. A dose-dependent increase in estradiol, progesterone, FSH, and LH concentrations was observed in rats treated with 100, 200, 400, and 800 mg/kg of the extrac respectively t. The highest dose (800 mg/kg) produced hormone concentrations comparable to those observed in the Vitamin C-treated and normal control groups.

Table 3.3. Serum reproductive hormone concentrations (Mean ± SD, n = 5).

Hormone	Normal Control	BPA Control	Vitamin C	DT100	DT200	DT400	DT800
Estradiol (pg/mL)	48.62 ± 2.81[a]	21.84 ± 1.62[e]	44.32 ± 2.54[b]	28.46 ± 1.91[d]	34.72 ± 2.12[c]	40.83 ± 2.36[b]	46.18 ± 2.63[a]
Progesterone (ng/mL)	18.45 ± 1.10[a]	8.41 ± 0.63[e]	16.62 ± 1.02[b]	10.84 ± 0.75[d]	13.42 ± 0.86[c]	15.76 ± 0.94[b]	17.83 ± 1.04[a]
FSH (mIU/mL)	6.12 ± 0.39[a]	2.84 ± 0.22[e]	5.61 ± 0.34[b]	3.71 ± 0.26[d]	4.42 ± 0.31[c]	5.14 ± 0.33[b]	5.92 ± 0.37[a]
LH (mIU/mL)	4.92 ± 0.34[a]	2.01 ± 0.16[e]	4.53 ± 0.29[b]	2.81 ± 0.19[d]	3.44 ± 0.24[c]	4.08 ± 0.27[b]	4.74 ± 0.31[a]

Different superscripts within the same row indicate significant differences ($p < 0.05$).

3.4. Effect of Aqueous Seed Extract of *D. tripetala* on Ovarian Microbial Load

Table 3.4 presents the ovarian microbial profile of female Wistar rats following exposure to Bisphenol A (BPA) and subsequent treatment with Vitamin C or aqueous seed extract of *D. tripetala* at doses of 100, 200, 400, and 800 mg/kg respectively. The BPA control group exhibited significantly higher total viable, coliform, and fungal counts than the normal control group ($p < 0.05$). Administration of Vitamin C markedly lowered these microbial counts. Similarly, treatment with the aqueous seed extract of D. tripetala produced significant reductions in all microbial parameters when compared with the BPA control group ($p < 0.05$). The antimicrobial effect of the extract improved progressively with increasing dose, with rats treated at 800 mg/kg showing the lowest microbial counts among the extract-treated groups and values comparable to those of the Vitamin C and normal control groups.

Table 3.4. Ovarian microbial counts (Mean ± SD, ×10³ CFU/g, n = 5).

Group	Total Viable Count	Coliform Count	Fungal Count
Normal Control	3.54 ± 0.28^{e}	0.96 ± 0.08^{e}	0.42 ± 0.05^{e}
BPA Control	10.82 ± 0.71^{a}	4.23 ± 0.31^{a}	2.14 ± 0.18^{a}
Vitamin C	4.31 ± 0.33^{d}	1.21 ± 0.10^{d}	0.61 ± 0.07^{d}
DT100	8.22 ± 0.62^{b}	3.11 ± 0.24^{b}	1.62 ± 0.14^{b}
DT200	6.84 ± 0.53^{c}	2.42 ± 0.19^{c}	1.18 ± 0.11^{c}
DT400	5.42 ± 0.46^{d}	1.71 ± 0.13^{d}	0.82 ± 0.08^{d}
DT800	4.02 ± 0.35^{d}	1.04 ± 0.09^{e}	0.51 ± 0.05^{e}

Different superscripts within the same column indicate significant differences ($p < 0.05$).

3.5. Microorganisms Isolated from Ovarian Tissues

Table 3.5 presents the bacterial and fungal isolates recovered from the ovarian tissues of female Wistar rats exposed to Bisphenol A (BPA) and treated with Vitamin C or aqueous seed extract of *D. tripetala* at doses of 100, 200, 400, and 800 mg/kg. A greater diversity of microbial isolates was observed in the BPA control group compared with the normal control group. The BPA-treated rats harboured multiple bacterial species, including *Escherichia coli*, *Staphylococcus aureus*, *Bacillus* spp., and *Proteus* spp., as well as fungal growth identified as *Candida* spp. Treatment with Vitamin C and the aqueous seed extract of *D. tripetala* reduced the occurrence and diversity of microbial isolates across the treatment groups. This reduction became more pronounced with increasing extract dose, with only *Bacillus* spp. detected at 400 mg/kg and no significant bacterial growth or fungal isolates observed in the 800 mg/kg treatment group.

Table 3.5. Microbial isolates recovered from ovarian tissues.

Group	Bacterial Isolates	Fungal Isolates
Normal Control	Bacillus spp.	Nil
BPA Control	*Escherichia coli*, *Staphylococcus aureus*, *Bacillus* spp., *Proteus* spp.	*Candida* spp.
Vitamin C	*Bacillus* spp.	Nil
DT100	*Staphylococcus aureus*, *Bacillus* spp.	*Candida* spp.
DT200	*Bacillus* spp., *Staphylococcus epidermidis*	Nil
DT400	*Bacillus* spp.	Nil
DT800	No significant bacterial growth	Nil

3.6. Histopathological Findings of the Ovary

Figure 2 shows the histopathological features of ovarian tissues from female Wistar rats exposed to Bisphenol A (BPA) and treated with Vitamin C or aqueous seed extract of *D. tripetala* at doses of 100, 200, 400, and 800 mg/kg respectively . The normal control group exhibited normal ovarian architecture, whereas the BPA control group

showed marked degenerative alterations, including follicular atresia, granulosa cell degeneration, vascular congestion, inflammatory cell infiltration, and stromal disruption. Treatment with Vitamin C and aqueous seed extract of *D. tripetala* improved ovarian histology in a dose-dependent manner. Mild histological improvement was observed at 100 mg/kg, while moderate restoration of ovarian architecture occurred at 200 mg/kg. More pronounced recovery was evident at 400 mg/kg, and the 800 mg/kg group displayed near-normal ovarian histoarchitecture comparable to that of the normal control and Vitamin C-treated groups.

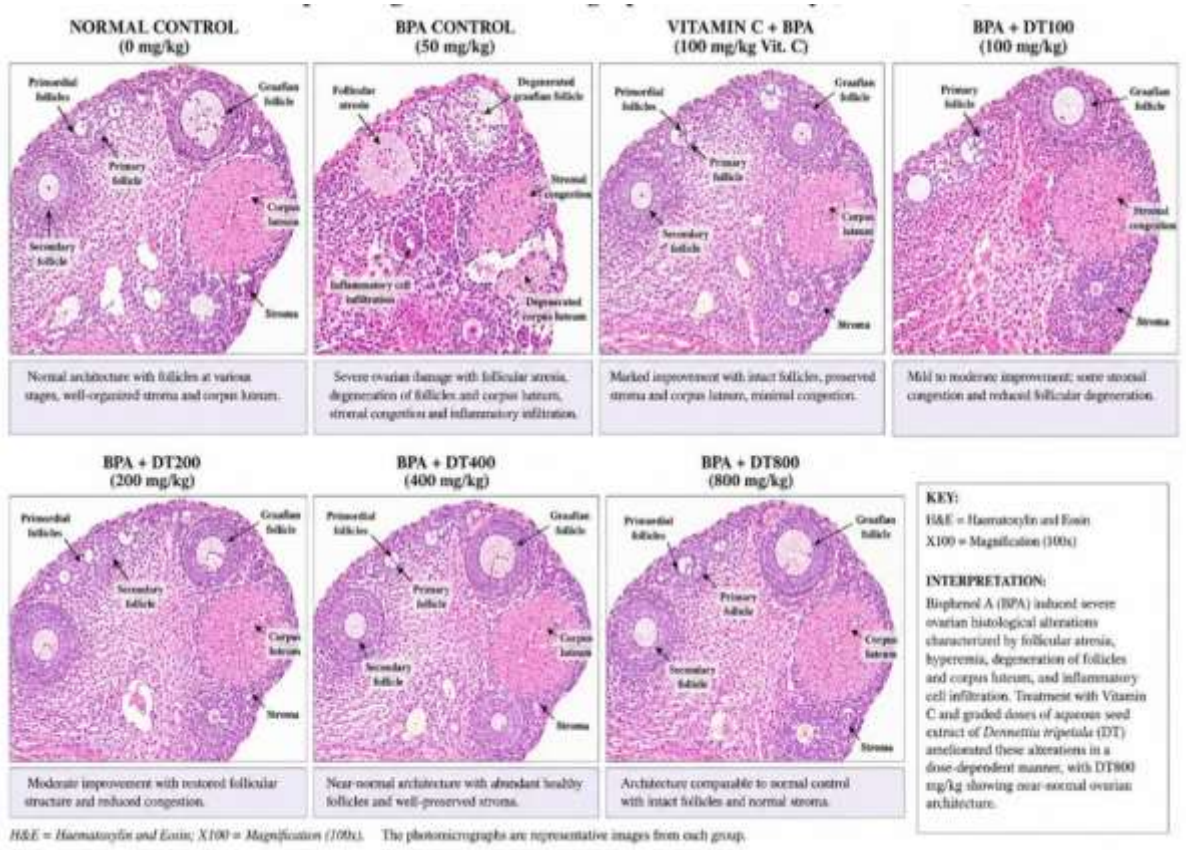

Figure 2. Histopathological photomicrographs of ovarian tissues from female Wistar rats exposed to Bisphenol A (BPA) and treated with graded doses of aqueous seed extract of *D. tripetala* (H&E, ×100).

Key: H&E = Hematoxylin and Eosin stain; ×100 = Magnification (100×); BPA = Bisphenol A; DT = Dennettia tripetala aqueous seed extract.

4. Discussion

4.1. Phytochemical Composition of Aqueous Seed Extract of *D. tripetala*

The phytochemical screening of the aqueous seed extract of *D. tripetala* revealed the presence of several bioactive constituents, including flavonoids, phenolic compounds, alkaloids, tannins, saponins, terpenoids, glycosides, and steroids. Among these constituents, flavonoids and phenolic compounds were the most abundant, while alkaloids, tannins, saponins, and terpenoids were moderately present. Glycosides and steroids were detected in lower amounts.

The presence of these phytochemicals suggests that the aqueous seed extract possesses a rich composition of secondary metabolites that may contribute to its biological activities as previously accounted by Nwanze et al. [37].

Flavonoids and phenolic compounds have been widely associated with antioxidant properties due to their ability to scavenge free radicals and reduce oxidative damage [6, 16]. Similarly, alkaloids, tannins, and saponins have been reported to possess anti-inflammatory [38], antimicrobial [39], and protective effects in biological systems [40], respectively. The occurrence of terpenoids, glycosides, and steroids further supports the therapeutic potential of the plant, as these compounds have been linked to various pharmacological activities [41-43]. The diverse phytochemical profile observed in the present study may therefore account for the protective effects of the extract against BPA-induced ovarian toxicity [44].

4.2. Protective Effect of Aqueous Seed Extract of *D. tripetala* on Ovarian Biochemical Parameters in BPA-Induced Oxidative Stress

The present study demonstrated that exposure to Bisphenol A (BPA) induced significant oxidative stress in the ovaries of female Wistar rats, as evidenced by elevated malondialdehyde (MDA) levels and decreased concentrations of reduced glutathione (GSH), superoxide dismutase (SOD), catalase (CAT), and total protein. These findings are consistent with previous reports indicating that BPA promotes excessive generation of reactive oxygen species (ROS), resulting in lipid peroxidation, cellular damage, and impairment of endogenous antioxidant defense systems [44, 45].

Treatment with aqueous seed extract of *D. tripetala* significantly attenuated these biochemical alterations in a dose-dependent manner. The observed reduction in MDA concentration suggests inhibition of lipid peroxidation and stabilization of cellular membranes, while the increases in GSH, SOD, and CAT indicate restoration of antioxidant defense mechanisms [4, 46. The highest extract dose produced effects comparable to those observed in the Vitamin C-treated group, suggesting strong antioxidant activity. These effects may be attributed to the abundance of flavonoids, phenolic compounds, alkaloids, and other phytochemicals present in *D. tripetala*, which are known to scavenge free radicals and enhance antioxidant enzyme activity [47]. Therefore, the extract appears to protect ovarian tissues against BPA-induced oxidative injury and preserve cellular homeostasis.

4.3. Protective Effect of Aqueous Seed Extract of *D. tripetala* on Reproductive Hormones in BPA-Induced Toxicity

Bisphenol A administration significantly reduced serum estradiol, progesterone, follicle-stimulating hormone (FSH), and luteinizing hormone (LH) concentrations compared with the normal control group. These findings support previous studies demonstrating that BPA acts as an endocrine-disrupting chemical capable of interfering with the hypothalamic-pituitary-ovarian axis and impairing steroidogenesis. Reduced concentrations of these hormones may adversely affect follicular development, ovulation, and fertility [48-50].

Administration of aqueous seed extract of *D. tripetala* significantly restored hormone concentrations toward normal values, with the highest dose showing results comparable to those of the Vitamin C-treated group. The improvement in hormonal status may be associated with the antioxidant properties of the extract, which likely protected ovarian follicles, granulosa cells, and steroidogenic tissues from oxidative damage [51]. The preservation of these structures may facilitate normal hormone synthesis and secretion. Consequently, the findings suggest that

D. tripetala possesses endocrine-supportive properties capable of mitigating BPA-induced reproductive dysfunction.

4.4. Protective Effect of Aqueous Seed Extract of *D. tripetala* on Ovarian Microbial Load

The present study revealed that BPA exposure increased ovarian microbial burden, as evidenced by elevated total viable count, coliform count, fungal count, and the presence of diverse bacterial and fungal isolates. Increased oxidative stress may compromise tissue integrity and local defense mechanisms, thereby creating conditions favorable for microbial colonization.

Treatment with aqueous seed extract of *D. tripetala* significantly reduced microbial counts and progressively eliminated microbial isolates in a dose-dependent manner. At the highest dose, no significant bacterial growth and no fungal isolates were observed. These findings are consistent with previous reports demonstrating the broad-spectrum antimicrobial activity of *D. tripetala* against several pathogenic microorganisms[37, 52, 53]. The antimicrobial effects may be attributed to phytochemicals such as tannins, flavonoids, alkaloids, and essential oils, which can disrupt microbial cell membranes, inhibit metabolic pathways, and suppress microbial proliferation. The ability of the extract to reduce microbial burden may contribute to the maintenance of a healthier ovarian microenvironment during oxidative stress conditions [52-54].

4.5. Protective Effect of Aqueous Seed Extract of *D. tripetala* on Ovarian Histoarchitecture

Histopathological examination revealed marked ovarian damage in BPA-treated rats, characterized by follicular atresia, degeneration of granulosa cells, vascular congestion, inflammatory cell infiltration, and disruption of normal stromal organization. These structural alterations are characteristic features of oxidative stress-mediated ovarian injury and may contribute to impaired reproductive function.

Conversely, treatment with aqueous seed extract of *D. tripetala* produced dose-dependent improvements in ovarian histology. Animals receiving higher doses exhibited preservation of follicular architecture, intact granulosa and theca cell layers, normal stromal organization, and absence of significant inflammatory lesions. The histological appearance of the 800 mg/kg group was comparable to that of the normal control and Vitamin C-treated groups. These observations suggest that the extract effectively protected ovarian tissues from BPA-induced morphological damage.

The histopathological findings corroborate the biochemical and hormonal results obtained in the present study. The restoration of antioxidant enzyme activities and reduction of oxidative damage likely contributed to the preservation of ovarian cellular integrity and follicular development [55, 56]. Furthermore, the reduced microbial burden may have minimised inflammatory responses, thereby enhancing tissue recovery and maintaining normal ovarian function [57].

Overall, the findings demonstrate that aqueous seed extract of *Dennettia tripetala* exerts significant antioxidant, endocrine-modulating, antimicrobial, and tissue-protective effects against BPA-induced ovarian toxicity in female Wistar rats.

5. Conclusion

The present study successfully evaluated the protective effects of aqueous seed extract of *D. tripetala* against Bisphenol A (BPA)-induced ovarian toxicity in female Wistar rats and comprehensively determined its phytochemical composition. Qualitative phytochemical screening clearly revealed the presence of flavonoids, phenolic compounds, alkaloids, tannins, saponins, terpenoids, glycosides, and steroids, thereby demonstrating the rich phytochemical nature of the extract. BPA exposure significantly and adversely affected ovarian function by inducing oxidative stress, disrupting reproductive hormone concentrations, increasing microbial burden, and causing histopathological damage to ovarian tissues. Conversely, treatment with aqueous seed extract of *D. tripetala* effectively and progressively ameliorated these alterations in a dose-dependent manner. Notably, the extract markedly improved ovarian biochemical parameters, substantially restored reproductive hormone concentrations, significantly reduced microbial counts and isolates, and histologically preserved ovarian tissue architecture. Furthermore, the highest dose of the extract produced the most pronounced protective effects and performed comparably to Vitamin C treatment. Overall, the findings strongly concluded that aqueous seed extract of *D. tripetala* possesses potent antioxidant, antimicrobial, endocrine-supportive, and ovarian protective activities and may therefore serve as a promising natural therapeutic agent for the effective management of BPA-induced reproductive toxicity and other oxidative stress-related ovarian disorders. Future studies should:

1. Isolate and identify the bioactive compounds responsible for the protective effects of *Dennettia tripetala* seed extract.
2. Conduct long-term toxicity and safety studies to establish the safety profile of *Dennettia tripetala* seed extract.
3. Investigate the molecular mechanisms underlying the antioxidant and ovarian protective activities of *Dennettia tripetala* seed extract.
4. Evaluate its protective effects of *Dennettia tripetala* seed extract against other environmental reproductive toxicants.
5. Conduct clinical trials to confirm efficacy of *Dennettia tripetala* seed extract and its safety in humans.
6. Develop standardised formulations of *Dennettia tripetala* seed extract for future therapeutic applications.

Declarations

Source of Funding

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Consent for Publication

The authors declare that they consented to the publication of this study.

Competing Interests

The authors declare that they have no competing interests.

Authors' Contribution

Owo, Gogo James conceived and designed the study. Okwelle, Achinike Austin., Owo, Gogo James., and Enyindah, Kingsley Chimene carried out the experimental work, collected and analyzed the data, and prepared the manuscript respectively. All authors read and approved the final manuscript.

Availability of Data and Materials

The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Ethical Approval

All experimental procedures involving animals were conducted in accordance with internationally accepted guidelines for the care and use of laboratory animals and were approved by the Animal Ethics Committee of the Department of Animal and Environmental Biology, Ignatius Ajuru University of Education, Rumuolumeni, Port Harcourt, Rivers State, Nigeria, prior to the commencement of the study (Approval No.: IAUE/FNAS/AEB/REC/2026/010).

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