

Phytochemical Characterisation and Histomorphological Evaluation of *Dubim* (*Gossypium barbadense* and *Ricinus communis*) Extract on the Pituitary Gland of Male Wistar Rats

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Abstract

Dubim is a traditional herbal preparation from north-central Nigeria, formulated from cotton seeds (*Gossypium barbadense*) and castor seeds (*Ricinus communis*) and used in ethnomedicine for fertility regulation. Despite its established traditional use, scientific evidence concerning its phytochemical composition and effects on reproductive endocrine tissues remains limited. This study profiled the phytochemical constituents of *Dubim* extract and evaluated its histomorphological effects on the pituitary gland of male Wistar rats following oral administration. Twenty, adult male Wistar rats were randomised into four groups (n = 5): control (distilled water) and treatment groups receiving 100, 300, or 500 mg/kg body weight of aqueous *Dubim* extract daily for 21 days. Pituitary glands were processed for Haematoxylin and Eosin (H&E), Periodic Acid–Schiff (PAS), and Cresyl violet staining. Qualitative phytochemical screening revealed alkaloids and saponins as predominant constituents, with flavonoids, glycosides, tannins, terpenoids, steroids, and oxalates detected at lower abundance. Histological examination demonstrated dose-dependent pituitary alterations, including progressive cellular disorganisation, chromophil depletion, and cytoplasmic vacuolation. PAS staining showed attenuation of glycoprotein-positive cells, consistent with diminished secretory activity, while cresyl violet staining revealed progressive loss of Nissl substance, suggestive of impaired protein synthetic capacity. These findings provide preliminary pharmacological evidence supporting the traditional use of *Dubim* in fertility regulation, while highlighting potential endocrine-disruptive effects at higher doses. Further studies incorporating quantitative morphometry, hormonal assays, and mechanistic investigations are warranted to confirm these observations and establish safe dosage parameters

Keywords: *Dubim*; Pituitary Gland; Male Fertility; *Gossypium Barbadense*; *Ricinus Communis*; Phytochemistry

1. Introduction

Medicinal plants have served as fundamental components of healthcare systems across human civilisations, with an estimated 80% of the world's population relying on traditional medicine for primary healthcare needs [1]. In Nigeria, ethnobotanical preparations remain deeply integrated into cultural practices and community health management, offering accessible and affordable therapeutic options [2]. Among these traditional remedies, fertility-regulating agents hold

considerable significance, as reproductive health concerns affect approximately 8-12% of couples globally, with male factors contributing to nearly half of all infertility cases [3].

Dubim is a traditional herbal preparation originating from the Ilorin emirate in north-central Nigeria, formulated from the seeds of cotton (*Gossypium barbadense*.) and castor (*Ricinus communis*). Ethnobotanical documentation indicates its use by traditional healers for fertility regulation, though whether for contraceptive or fertility-enhancing purposes appears to vary according to dosage and preparation methods. Both constituent

plants possess well-documented bioactive properties: *Gossypium barbadense* contain *gossypol*, a polyphenolic compound extensively studied for its antispermato-genic effects [4], while *Ricinus communis* has been associated with anti-implantation activity and reversible suppression of spermatogenesis in experimental studies [5, 6].

Reproductive function in males is orchestrated through the hypothalamic-pituitary-gonadal (HPG) axis, a neuroendocrine system wherein the pituitary gland serves as a critical interface between central nervous system input and peripheral endocrine output [7]. The anterior pituitary synthesizes and secretes the glycoprotein gonadotropins, luteinizing hormone (LH) and follicle-stimulating hormone (FSH), which are essential for testicular steroidogenesis and spermatogenesis [8]. Structural or functional impairment of pituitary gonadotrophs may therefore substantially compromise male fertility, making this gland a relevant target for evaluating both contraceptive agents and potential reproductive toxicants [9, 10]. Histopathological and histochemical techniques provide valuable tools for assessing tissue-level responses to pharmacological interventions. Haematoxylin and Eosin (H&E) staining permits evaluation of cellular organisation, chromophil integrity, and tissue architecture [11]. Periodic Acid Schiff (PAS) staining selectively visualises glycoproteins, including the carbohydrate moieties of gonadotropin hormones, thereby providing insight into secretory activity and cell-type differentiation within the anterior pituitary [12]. Cresyl Violet staining demonstrates Nissl substance, reflecting ribosomal RNA content and cellular protein synthetic capacity, which is particularly relevant for endocrine cells engaged in active hormone production [13].

Despite the widespread traditional use of *Dubim*, there is a paucity of scientific evidence documenting its phytochemical composition and effects on reproductive endocrine tissues [15]. Understanding these effects is necessary not only for validating traditional claims but also for establishing safety profiles that may inform rational therapeutic application. The present study therefore aimed to profile the phytochemical constituents of *Dubim* extract using qualitative screening methods, and to evaluate the histomorphological effects of sub-chronic *Dubim* administration on the pituitary gland of male Wistar rats.

2. Materials and Methodology

2.1 Plant material and preparation of *Dubim* extract

Dubim was prepared from authenticated cotton seeds (*Gossypium barbadense*.) and castor seeds (*Ricinus communis*) following the traditional preparation method documented during ethnobotanical inquiry. Seeds were obtained from Pakata Market, Ilorin West Local Government Area of Kwara

State, Nigeria, and authenticated by a taxonomist at the Herbarium Unit, Department of Botany, Faculty of Life Sciences, University of Ilorin, Nigeria Voucher Number *Gossypium barbadense* UILH\001\977\ 2025 and *Ricinus communis*: UILH\002\965\2025. The plant material was air-dried under shade at room temperature for 10 days and ground into fine powder using a mechanical grinder. The powder was stored in air-tight containers prior to extraction [16].

20 g of combined powdered material (1:1) was subjected to aqueous maceration at a 1:10 (w/v) ratio for 72 hours with intermittent shaking [17]. The mixture was filtered through Whatman No. 1 filter paper and the filtrate concentrated using a water-bath at a controlled temperature of 40 degrees C. The extract was prepared following standard procedures as documented by earlier researchers [2] and stored appropriately prior to administration.

2.2 Phytochemical screening

Qualitative phytochemical screening of *Dubim* extract was performed using established standard procedures to detect major classes of secondary metabolites, including flavonoids, tannins, saponins, glycosides, phenolic compounds, alkaloids, terpenoids, steroids, and oxalates [17]. Semi-quantitative estimation of the relative abundance of each class was recorded using a three-tier grading system: (+++) indicating high abundance, (++) indicating moderate abundance, and (+) indicating low abundance, based on the intensity of the characteristic reactions observed.

2.3 Experimental animals and study design

Twenty, adult male Wistar rats weighing an average of 200g each were used in this study. Animals were housed under standard laboratory conditions with controlled temperature (22-25 degrees C), humidity (50-60%), and a 12-hour light/dark cycle. They were allowed free access to standard rat chow and water and were acclimatised for two weeks before commencement of treatment [18]. Rats were randomly assigned into four groups of five animals each. The control group received distilled water by oral gavage, while treatment groups received *Dubim* extract at 100, 300, and 500 mg/kg body weight daily for three weeks [19]. The doses used were adapted from previous sub-chronic toxicity studies involving related plant extracts, with the lowest dose based on reported traditional usage levels and the higher doses established to delineate a dose-response relationship [19, 20].

2.4 Tissue collection and processing

At the end of the treatment period, animals were humanely sacrificed by cervical dislocation under anaesthesia. Pituitary glands were excised promptly, trimmed of surrounding

connective tissue, and fixed in 10% neutral buffered formalin for 24 hours. Tissues were processed routinely, embedded in paraffin wax, and serially sectioned at approximately 5 micrometres using a rotary microtome. Sections were mounted on clean glass slides and prepared for staining [11].

2.5 Histological and histochemical staining

Sections were stained with Haematoxylin and Eosin (H&E) for general histoarchitectural assessment. Periodic Acid Schiff (PAS) staining was performed to evaluate glycoprotein distribution and secretory activity. Cresyl Violet staining was applied to assess Nissl substance and cellular protein synthetic capacity. All staining procedures followed standard histological protocols [16].

2.6 Histomorphological evaluation

Stained sections were examined under a light microscope (Olympus CX23, Japan) by two experienced morphologist and results were compared. All discrepancies were resolved using a third observer. Photomicrographs were captured for documentation at x100 and x400 magnification. Qualitative assessment was focused on cellular organisation, chromophil integrity, tissue architecture, and staining intensity. Histopathological changes were recorded and summarised according to severity and dose-response pattern, following established toxicologic pathology guidelines [18, 20]. Semi-quantitative grading of histopathological changes was applied as follows: absent (0), mild (+), moderate (++), and severe (+++).

3. Results

3.1 Extraction yield and phytochemical profile of *Dubim* extract

The aqueous extraction of *Dubim* yielded approximately 12 % [9.2% and 15.2% of *Gossypium barbadense*. and *Ricinus communis*] of dry extract, reflecting the solubility of active constituents in the aqueous solvent. Qualitative phytochemical screening revealed a diverse range of secondary metabolites in the *Dubim* extract. Alkaloids and saponins were the most abundant constituents, followed by flavonoids and glycosides at moderate levels. Tannins, terpenoids, steroids, and oxalates were also detected, though at lower relative abundance. The results of the preliminary phytochemical screening are summarised in Table 1.

3.2 Histopathological effects of *Dubim* extract on pituitary architecture (H&E staining)

Haematoxylin and Eosin-stained sections of pituitary glands (Plate 1 A-D) demonstrated well-preserved anterior pituitary architecture characterised by organised cellular cords and nests of endocrine cells separated by delicate sinusoidal capillaries in

the control group (Plate 1A). Acidophils, consistent with somatotrophs and lactotrophs, were identified by their eosinophilic cytoplasm. Basophilic cells, likely representing gonadotrophs, thyrotrophs, or corticotrophs, displayed deeply-staining cytoplasm, and chromophobes appeared as pale-staining cells with scant cytoplasm. No cellular atypia, necrosis, or architectural distortion was observed in control sections. Cells were densely packed with clearly defined cytoplasmic and nuclear features.

In contrast, pituitary glands from *Dubim*-treated rats exhibited dose-dependent histomorphological alterations. At 100 mg/kg (1B, low dose), mild cellular disorganisation with early chromophil depletion and a slight reduction in cellular density were observed. At 300 mg/kg (1C, moderate dose), more pronounced architectural distortion was evident, characterised by disruption of cellular cords, cytoplasmic vacuolation, and noticeable chromophil depletion. At 500 mg/kg (1D, high dose), severe alterations were present, including extensive chromophil loss, cellular rarefaction, widespread tissue disorganisation, and cells with poorly-defined nuclear contours and reduced intercellular cohesion. A semi-quantitative summary of these findings is presented in Table 2.

Table 1: Preliminary phytochemical screening of *Dubim* extract

S/N	Phytochemical	Qualitative result	Detection method	Positive indication
1	Alkaloids	+++	Dragendorff's reagent	Orange precipitate
2	Flavonoids	++	Shinoda test	Pink/red colouration
3	Saponins	+++	Frothing test	Persistent foam
4	Tannins	+	Ferric chloride (FeCl ₃) test	Blue/green-black colouration
5	Glycosides	++	Keller-Killiani test	Brown ring formation
6	Terpenoids	+	Salkowski test	Reddish-brown interface
7	Oxalates	+	Calcium chloride (CaCl ₂) test	White precipitate
8	Steroids	+	Liebermann-Burchard test	Blue-green colouration

+++ , high abundance; ++ , moderate abundance; + , low abundance

3.3 Periodic Acid Schiff histochemical findings

PAS-stained sections from control animals showed heterogeneous positivity consistent with the normal functional diversity of the anterior pituitary. Cells with moderate-to-strong

PAS-positive granular cytoplasm, suggestive of basophilic gonadotrophs containing glycosylated hormone precursors, were clearly identified. Chromophobes and acidophilic cells exhibited low-to-absent PAS reactivity, reflecting normal cytological heterogeneity. No architectural distortion, necrosis, or inflammatory changes were observed in control sections.

In *Dubim*-treated groups, PAS staining intensity was progressively attenuated in a dose-dependent manner. At the low dose, scattered cells retained focal PAS reactivity, suggesting that some secretory cell populations maintained partial activity while others appeared compromised. At the moderate and high doses, a marked reduction in PAS-positive cells was observed, with the high-dose group showing predominantly negative or faintly reactive cytoplasm throughout. These observations are consistent with a reduction in glycoprotein hormone content, which may reflect either decreased cell numbers, reduced synthetic activity in remaining cells, or both as shown in PAS photomicrographs in Plate 2.

Table 2. Semi-quantitative grading of pituitary glands histomorphology

Parameter	Control	100 mg/kg	300 mg/kg	500 mg/kg
Cellular disorganisation (H&E)	0	+	++	+++
Chromophil depletion (H&E)	0	+	++	+++
Cytoplasmic vacuolation (H&E)	0	0	+	++

0, absent; +, mild; ++, moderate; +++, severe

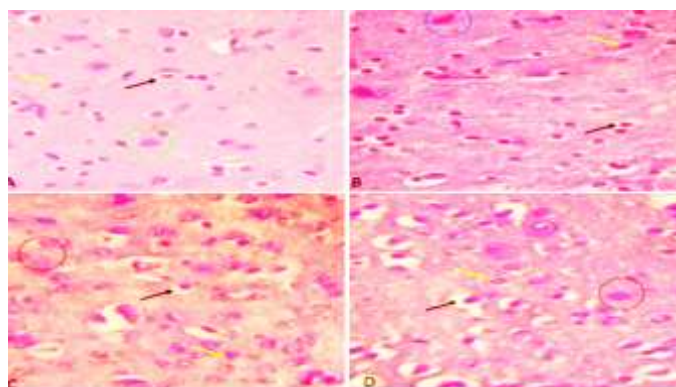


Plate 1: Histological slides of the male pituitary gland (H&E stain), x100. Control (A); 100 mg/kg, low dose (B); 300 mg/kg, moderate dose (C); 500 mg/kg, high dose (D).

3.4 Cresyl Violet histochemical findings

Cresyl Violet-stained sections from control animals demonstrated prominent, coarsely-granular Nissl substance in endocrine cells consistent with active protein synthesis. Cells with abundant violet-staining cytoplasm, likely representing functionally active basophils such as corticotrophs and

gonadotrophs, were readily identified alongside chromophobes showing minimal staining, reflecting a normal range of synthetic activity within the gland.

Dubim-treated groups showed a progressive reduction in Cresyl Violet staining intensity with increasing dose. At the low dose, partial attenuation was observed, with some cells retaining prominent Nissl granules while others appeared pale. The moderate dose group exhibited a more uniform reduction in basophilic cytoplasmic staining. At the high dose, extensive loss of Nissl substance was seen throughout the section, with pale, chromophobe-like cytoplasm predominating, consistent with impaired synthetic capacity or cellular exhaustion. The Cresyl Violet photomicrographs are presented in Plate 3.

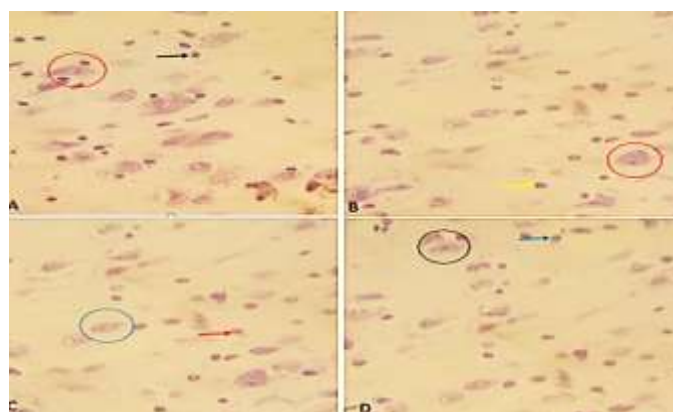


Plate 2: Histological slides of the male pituitary gland (PAS stain), x100. Control (A); 100 mg/kg, low dose (B); 300 mg/kg, moderate dose (C); 500 mg/kg, high dose (D).

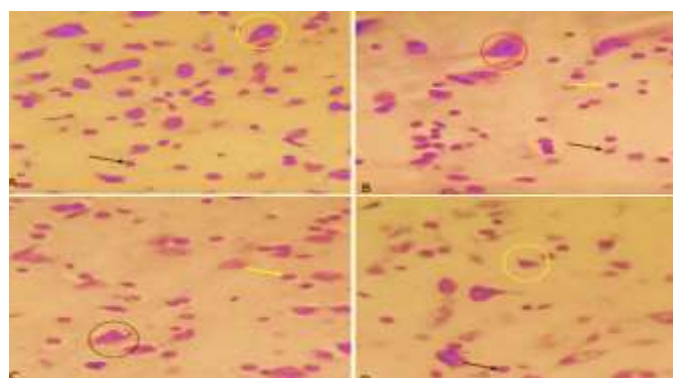


Plate 3: Histological slides of the male pituitary gland (Cresyl Violet stain), x100. Control (A); 100 mg/kg, low dose (B); 300 mg/kg, moderate dose (C); 500 mg/kg, high dose (D).

Discussion

The present study investigated the phytochemical composition of *Dubim*, a traditional herbal preparation combining *Gossypium barbadense* and *Ricinus communis* seeds, and assessed its histomorphological effects on the pituitary gland of male Wistar rats. The findings suggest that *Dubim* extract contains diverse bioactive phytochemicals and may induce dose-dependent morphological and histochemical alterations in pituitary architecture, secretory activity, and protein synthetic

capacity. These results provide preliminary pharmacological evidence broadly consistent with the ethnopharmacological use of *Dubim* in fertility regulation, while raising important safety considerations at higher doses.

Table 3: Semi-quantitative grading of histomorphological changes in pituitary glands

Parameter	Control	100 mg/kg	300 mg/kg	500 mg/kg
Reduction in PAS positivity	0	+	++	+++
Reduction in Nissl substance (Cresyl Violet)	0	+	++	+++

0, absent; +, mild; ++, moderate; +++, severe

Phytochemical Composition and Bioactive Implications

Qualitative phytochemical screening of *Dubim* extract revealed alkaloids and saponins as the most abundant secondary metabolites, followed by flavonoids and glycosides at moderate levels, with tannins, terpenoids, steroids, and oxalates detected at lower abundance. This profile aligns with the reported phytochemical diversity of both constituent plants, recognised as rich sources of biologically active compounds [6,7].

The predominance of alkaloids is noteworthy given their documented reproductive effects. *Gossypol*, the principal polyphenolic compound in cotton seeds, has been extensively studied for anti-spermatogenic properties, including inhibition of sperm motility, disruption of spermatogenesis, and suppression of testicular enzyme activity [8,9]. *Gossypol* acts partly through inhibition of lactate dehydrogenase-X (LDH-X), an enzyme central to sperm energy metabolism, and through interference with mitochondrial function in germ cells [10]. The presence of alkaloids in *Dubim* may therefore contribute to its fertility-regulating potential.

Saponins, also detected in high abundance, exhibit established effects on reproductive function, including spermicidal activity, interference with steroid hormone synthesis, and modulation of gonadotropin secretion through interactions with cholesterol-containing membranes and steroidogenic enzyme systems [11]. The membrane-active properties of saponins may also contribute to the cellular alterations observed in pituitary sections, as these compounds can influence membrane fluidity, receptor function, and signal transduction pathways relevant to endocrine cell activity [12].

Flavonoids and glycosides, present at moderate levels, possess antioxidant properties that may protect reproductive tissues from oxidative damage under some conditions. However, the dose-dependent histopathological changes observed suggest

that at higher concentrations, the combined bioactive load of *Dubim* may exert cytotoxic effects that outweigh any protective capacity [13]. The detection of oxalates at low levels also warrants consideration given their documented association with tissue irritation in experimental models.

Dose-Dependent Histomorphological Alterations in Pituitary Architecture

Histological examination of H&E-stained sections revealed progressive, dose-dependent architectural changes in *Dubim*-treated animals. Control sections showed well-organised cellular cords with intact acidophils, basophils, and chromophobes, consistent with normal anterior pituitary morphology. Treated groups demonstrated increasing degrees of cellular disorganisation, chromophil depletion, cytoplasmic vacuolation, and reduced cellular density, suggesting dose-dependent effects on pituitary cytoarchitecture.

Chromophil depletion affecting both acidophil and basophil populations is of particular relevance, as these cells represent the functional units of anterior pituitary hormone production. Acidophils (somatotrophs and lactotrophs) secrete growth hormone and prolactin, while basophils (gonadotrophs, thyrotrophs, and corticotrophs) produce the glycoprotein hormones luteinising hormone (LH), follicle-stimulating hormone (FSH), and thyroid-stimulating hormone. Degeneration or depletion of these cell populations would be expected to impair downstream endocrine function. The cytoplasmic vacuolation noted at moderate and high doses is consistent with cellular stress, potentially reflecting endoplasmic reticulum dilation or early degenerative processes [14]. Definitive cell-type identification requires immunohistochemical confirmation; the assignments described here are based on morphological characteristics under light microscopy.

The precise mechanisms underlying these histomorphological changes remain to be established. Bioactive compounds in *Dubim* may directly affect pituitary cells through oxidative stress, membrane disruption, or mitochondrial dysfunction. Alternatively, *Dubim* constituents may indirectly alter pituitary function by interfering with hypothalamic gonadotropin-releasing hormone (GnRH) secretion [15], disrupting peripheral endocrine feedback, or both [16].

PAS Staining and Possible Effects on Secretory Activity

PAS staining, which selectively visualises glycoproteins including the carbohydrate moieties of LH, FSH, and thyroid-stimulating hormone, revealed dose-dependent attenuation of staining intensity in *Dubim*-treated animals. Control sections demonstrated robust Periodic Acid Schiff-positive reactivity in

basophilic cells, consistent with active glycoprotein hormone synthesis. Treated groups showed progressive reduction in Periodic Acid Schiff reactivity, with the high-dose group exhibiting predominantly negative or faintly reactive cytoplasm. These observations are consistent with either a reduction in hormone-producing cell numbers, diminished synthetic activity in remaining cells, or impaired glycosylation of hormone precursors.

Periodic Acid Schiff findings should be interpreted with appropriate caution. Periodic Acid Schiff staining detects all glycoproteins and glycoconjugates and does not distinguish between specific hormone types. It cannot quantify hormone concentrations, and reduced staining may reflect a range of conditions from active secretion (with depleted intracellular stores) to reduced synthesis. Furthermore, Periodic Acid Schiff reactivity provides indirect evidence of secretory activity and is not a substitute for direct hormone assay. The observations described here are therefore best characterised as suggestive of possible impairment of glycoprotein hormone synthesis, pending corroboration by hormonal assays in future studies.

Cresyl Violet Staining and Possible Effects on Protein Synthetic Capacity

Cresyl violet staining, which demonstrates Nissl substance (rough endoplasmic reticulum and associated ribosomes), provides an indirect histochemical indication of cellular protein synthetic activity. Control pituitary sections showed prominent, coarsely granular Nissl substance in active endocrine cells. *Dubim*-treated animals demonstrated progressive attenuation of Nissl staining intensity, with the high-dose group showing extensive loss of basophilic cytoplasm consistent with possible impairment of protein synthesis. These findings parallel the PAS results and together suggest that *Dubim* may affect fundamental synthetic processes in pituitary endocrine cells.

As with PAS staining, cresyl violet findings should be regarded as suggestive rather than definitive. Nissl substance reduction may reflect cellular exhaustion, reduced transcriptional demand, or direct cytotoxicity, and the relative contribution of each pathway cannot be established from histochemical data alone. Direct measurement of ribosomal function, mRNA expression, or protein synthesis rates would be required to confirm these observations at the molecular level [17,18].

Correlation with Traditional Use and Fertility Implications

The observed pituitary effects are broadly consistent with the traditional use of *Dubim* in fertility regulation. Dose-dependent alterations in pituitary architecture, combined with findings suggestive of reduced glycoprotein hormone synthesis and diminished synthetic capacity, raise the possibility that *Dubim*

administration could reduce circulating gonadotropin levels and consequently suppress testicular function. These observations align with reported antifertility activities of both constituent plants [8–10].

However, the severity of histopathological changes at higher doses raises important safety considerations. While mild pituitary modulation might conceivably underlie a contraceptive effect, the extensive chromophil depletion and tissue disorganisation observed at 500 mg/kg suggest the possibility of more severe and potentially irreversible effects at this dose. The reversibility of these changes remains unknown and warrants investigation through recovery-period studies. Traditional practitioners' emphasis on specific dosage and preparation methods may reflect empirical recognition of a narrow therapeutic margin, underscoring the importance of documenting indigenous knowledge alongside formal scientific investigation.

Comparative Context and Study Limitations

The present findings are consistent with previous studies reporting reproductive effects of constituent plant species. reported anti-implantation activity in female rats following castor seed extract administration [19], while *Rajeh et al.* demonstrated reversible suppression of spermatogenesis in male mice treated with *Ricinus communis* leaf extract [20]. Studies on *gossypol* have documented direct testicular effects including germ cell degeneration and Sertoli cell disruption [10], with some investigators reporting changes in serum LH and FSH concentrations [21], though findings have been inconsistent across studies. The present study extends the evidence base by identifying the pituitary gland as a possible target organ for the effects of *Dubim*, though this requires confirmation.

Several limitations of the present study should be acknowledged. The sample size of $n = 5$ per group, while adequate for preliminary histomorphological assessment, limits statistical power for detecting subtle effects; findings should therefore be regarded as preliminary and hypothesis-generating. The absence of hormone assays means that the functional consequences of the observed histomorphological changes cannot be confirmed. The assessment was entirely qualitative and observer-dependent; quantitative morphometric analysis, including cell density counts and optical densitometry for PAS and cresyl violet staining, would strengthen future work. Extract standardisation was not performed and yield data were not fully documented, representing a pharmacological limitation. Additionally, this study was limited to male rats examined at a single time point, precluding assessment of reversibility or sex-specific effects. Future studies should

address these limitations through larger cohorts, extended treatment and recovery periods, hormone quantification, quantitative histomorphometry, and molecular mechanistic investigations [22,23].

Conclusion

Dubim extract contains diverse phytochemical constituents, with alkaloids and saponins identified as the most abundant secondary metabolites. Sub-chronic oral administration of *Dubim* extract at doses of 100, 300, and 500 mg/kg body weight induced dose-dependent histomorphological alterations in the pituitary gland of male Wistar rats, including progressive cellular disorganisation, chromophil depletion, and findings consistent with possible impairment of glycoprotein hormone synthesis and protein synthetic capacity. These preliminary observations are broadly consistent with the ethnopharmacological use of *Dubim* for fertility regulation and suggest that the pituitary gland may represent a target for its biological effects. Given the limitations of the present study, these findings should be regarded as preliminary. Further investigations incorporating quantitative morphometry, hormonal assays, and mechanistic studies are warranted to characterise the nature, extent, and reversibility of these effects, and to establish safe and effective dosage parameters.

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Availability of data and materials

Data generated during and analysed during the course of this study are available from the corresponding author on request.

Declaration of ethical approval

All animal experiments were performed in strict accordance with international and institutional ethical standards. The study adhered to the ARRIVE guidelines [15] and the NIH Guide for the Care and Use of Laboratory Animals, and was formally approved by the Institutional Animal Care and Use Committee (IACUC) of the College of Health Sciences, Joseph Ayo Babalola University, Arakeji, Osun State, Nigeria (Approval No. JABU\CHS\1A\059). All procedures prioritized animal welfare, minimizing pain and distress throughout the study.

Competing interests

Authors declare no competing interests

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