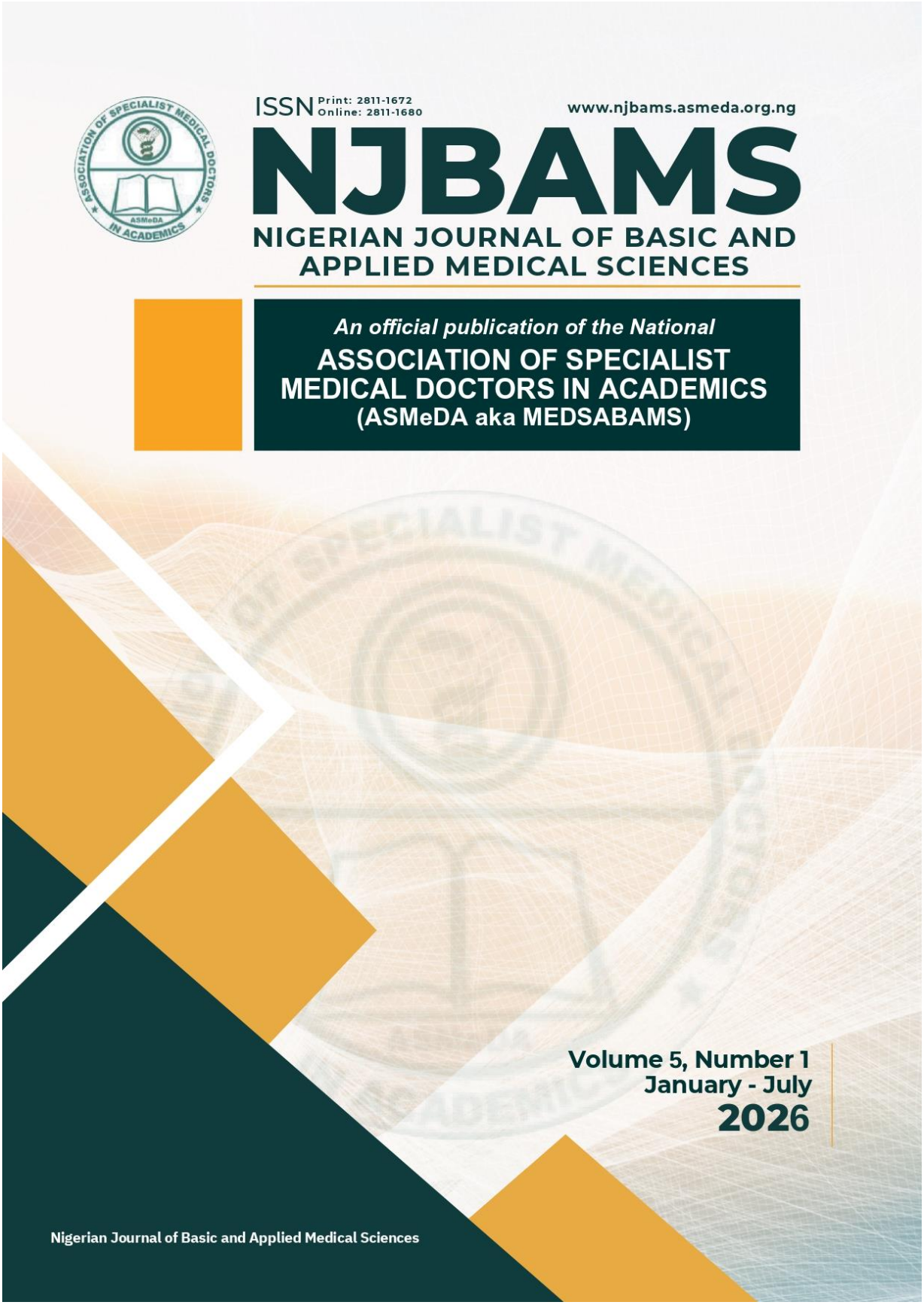

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Metabolic Effect of Herbal Antifibroid Decoction and Depo Provera in Pregnant Rabbits

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ABSTRACT

Background: Herbal antifibroid decoction is used in Nigeria for the treatment of fibroid, infertility and related diseases. The fresh samples of these medicinal plants, *Crysophyllum delevoyi, Cassia tora*, *Anthocleista djalonensis (root* and bark), *Blighia sapida* (Bark), *Citrullus colocynthis,* and *Xylopia aethiopica, which constitute the antifibroid decoction, were* purchased from Mushin market in Lagos.

Methods: They were identified and authenticated. Parts of these plants were cut into pieces and weighed. These were boiled in a pot containing 25 litres of distilled water for 90 minutes. The solution was allowed to cool and decanted. Concentrations of 40mg/kg and 20mg/kg were obtained from the stock. Twenty acclimatized and pregnant rabbits were divided into 4 groups. 2 Groups received varied doses of anti-fibroid decoction orally from the 15th day of gestation for twelve days. Group 3 received an intramuscular injection of Depo Provera, while group 4 was drug-free control. Fasting blood serum from all animals was analyzed using standard protocols. Results were analyzed using ANOVA and Student's T test.

Results: The antifibroid decoction reduced serum total cholesterol, triglycerides, and LDL cholesterol, but HDL cholesterol levels remained unchanged in all groups.

Conclusion: The albumin increased in the Depo Provera group, but the value reduced at the higher dose of the decoction.

Keywords: antifibroids, decoction, Depo provera, pregnant rabbits

INTRODUCTION

Medicinal plants have long played a crucial role in healthcare systems across both developing and developed nations, serving as important sources of therapeutic agents. The use of naturally derived compounds from plants in herbal remedies continues to contribute significantly to global wellness and disease management (1). Since ancient times, higher plants have been instrumental in supporting human health, and they remain essential in many traditional healthcare practices today. According to the World Health Organization, approximately 80% of the population in developing countries relies on traditional medicine, primarily plant-based therapies, for their primary healthcare needs (2, 3). Safety concerns for the fetus have been raised about the dangerous effects of the use of herbal medicines during pregnancy, especially in the first 3 months and in the third trimester (4). Despite the lack of evidence supporting the safety and clinical efficacy of herbal medicine (HM), its use among pregnant women continues to increase (5, 6). Given the high prevalence of contraindicated herbs among the pregnant population in the world, it is crucial to examine the use of HM and evaluate its safety

to ensure that women are using HM appropriately (4). Hence, proper consultation with the doctor and the pharmacist is necessary to ensure that the herbs are safe and suitable to use during pregnancy (4,5,6).

Several medicinal plants are traditionally believed to possess antifibroid properties and are used in the preparation of herbal decoctions. *Blighia sapida*, commonly known as ackee or “Isin” in some local dialects, is an evergreen tree from the family Sapindaceae that grows up to 10–12 meters in height (7). While the edible arils of its fruit are well known, its bark pulp is traditionally used in Ivory Coast for managing oedema and intercostal pain. Additionally, the pulp and leaves are applied as eye drops to treat ophthalmic conditions such as conjunctivitis (8,9).

Xylopia aethiopica, a member of the Annonaceae family, is another plant widely employed in traditional medicine. Its fruits, bark, leaves, and seeds are used in treating various ailments, including bronchitis, dysentery, asthma, stomach pain, cough, amenorrhea, and rheumatism (10, 11). In Ivory Coast, it is recommended to postpartum women as a tonic and to promote fertility and ease childbirth (8, 12). In Ghana, it has also been combined with *Newbouldia laevis* (family Bignoniaceae) to enhance menstrual flow, with reported abortifacient properties (11, 13).

Citrullus colocynthis (family Cucurbitaceae) is utilized for its seeds, roots, and fruits in managing various conditions. It possesses antimicrobial, purgative, anthelmintic, and contraceptive properties (14). *Cassia tora* Linn (family Leguminosae) is traditionally employed as a laxative, antiperiodic, anthelmintic, ophthalmic remedy, liver and cardiac tonic, and expectorant (15,16). It is also applied in the treatment of leprosy, skin disorders, and cancer therapy (17, 18).

Anthocleista djalonensis is another plant widely used in ethnomedicine for its antipyretic (fever-reducing), stomachic (digestive-aiding), analgesic (pain-relieving), and purgative (laxative) properties (19). Its root decoction is traditionally used in the treatment of diabetes mellitus, while the leaves are employed in managing malaria and jaundice. The bark, when used in small doses, serves as a purgative, but higher doses are considered toxic. In Sierra Leone, the leaf decoction is consumed for jaundice, whereas in Ivory Coast, the root is used as a diuretic, a vigorous purgative, and an antidote to poisons. It is also
applied in treating leprosy, edema, scrotal elephantiasis, and as an emmenagogue (agent that stimulates menstruation). The root decoction is similarly used to relieve chest pain, constipation, and abdominal discomfort (19, 20).

Chrysophyllum delevoyi De Wild, from the family Sapotaceae and commonly referred to as the African star apple, is used in managing gastrointestinal disorders such as diarrhea and dysentery, among other traditional applications (21).

In contrast to these herbal remedies, medroxyprogesterone acetate (commonly known as Depo Provera) is a synthetic, injectable contraceptive belonging to the class of progestins. It is also utilized in the clinical management of uterine fibroids, especially for symptomatic relief (22).

Despite the widespread use of herbal antifibroid decoctions by local populations as a cost-effective and accessible alternative to conventional treatments such as Depo Provera and mifepristone (RU-486), there is limited scientific data regarding their metabolic implications. This study aims to investigate the influence of a traditional herbal antifibroid decoction, as formulated by indigenous practitioners, on lipid, protein, and glucose profiles in pregnant rabbits. The rabbit model provides a relevant experimental platform for evaluating the safety and potential systemic effects of such preparations during pregnancy.

MATERIALS AND METHODS

Preparation of samples and decoction

Medicinal plants such as *Chrysophyllum delevoyi*, *Cassia tora*, *Anthocleista djalonensis* (root and bark), *Blighia sapida* (bark), *Citrullus colocynthis*, and *Xylopia aethiopica* were purchased from Mushin Market in Lagos, Nigeria. The plant materials were authenticated and identified at the Department of Botany and Microbiology, University of Lagos. Voucher specimens were deposited in the herbarium.

A total of 1 kg each of *Chrysophyllum delevoyi*, *Cassia tora*, and *Anthocleista djalonensis* (root and bark), 500 g of *Blighia sapida* (bark), and 800 g each of *Citrullus colocynthis* and *Xylopia aethiopica* were weighed and placed into a large pot. The herbs were washed thoroughly with water, soaked in 24 litres of distilled water, and boiled for 90 minutes. After cooling, 5 litres of the decoction were decanted. The decoction was stored in an airtight container and refrigerated until use, following the instructions of the traditional herbalist.

Chemicals and reagents

Medroxyprogesterone acetate (Depo Provera), 150 mg/mL (NAFDAC Reg. No. 01-2310), was obtained from the University Community Pharmacy, College of Medicine, University of Lagos (CMUL), Idi-Araba. All other chemicals used were standard laboratory reagents and solvents of Analar grade, procured from registered distributors.

Treatment of animals

The study involving experimental animals was conducted in accordance with internationally accepted principles for the use and care of laboratory animals (23) and with the permission of the university ethical committee. Twenty female and five male Dutch White rabbits, weighing between 1.5–1.55 ± 0.15 kg, were obtained from the Laboratory Animal Centre of the College of Medicine, University of Lagos. The female rabbits were randomly assigned to four groups, while the males were housed separately. Each group was kept in a metallic cage in the metabolic laboratory under controlled temperature conditions and a 12-hour light/dark cycle. Female rabbits were monitored for signs of estrus, including restlessness and vulvar swelling. Those in heat were introduced into the male cages for mating and then returned to their original cages upon confirmation of mating. The mating date was recorded for each rabbit. On day 14 post-mating (mid-gestation), Groups 1 and 2 received 1 mL of 40 mg and 20 mg of the herbal decoction, respectively, administered orally for 12 consecutive days. Group 3 received a single intramuscular injection of 1 mL of Depo Provera (2.73 mg/kg). Group 4 received 1 mL of distilled water and served as the control. Following the last administration, all animals were fasted overnight (18 hours) and subsequently sacrificed under diethyl ether anesthesia. The rabbits were fed standard rabbit pellets (Niemeth Livestock Feeds, Ikeja) and had access to water *ad libitum* throughout the experimental period.

Blood samples were collected via cardiac puncture into sterile, non-heparinized tubes and allowed to clot at room temperature. The clots were removed, and the samples were centrifuged at 2,500 g for 10 minutes to obtain fasting serum. Serum samples from each group were stored in a bio freezer until biochemical analysis. Fasting serum levels of albumin, globulins, total protein, urea, glucose, total cholesterol, triacylglycerol (TGL), high-density lipoprotein (HDL), and low-density lipoprotein (LDL) cholesterol were determined using Randox Laboratory kit reagents. Very low-density lipoprotein (VLDL) cholesterol was calculated using the formula: TGL ÷ 2.2 (mmol/L). LDL cholesterol was estimated by subtracting the sum of the HDL, VLDL, and intermediate-density lipoprotein (IDL) cholesterol fractions from the total cholesterol (24,25).

Statistical Analysis

The results are expressed as mean ± SD of 5 determinations. Statistical analysis was carried out between the groups and the control using Student's t-test, analysis of variance (Anova) and post hoc tests. A (p<0.05) was considered statistically significant when tests are compared with the controls.

RESULTS

The results showed that serum total protein, globulin, and urea concentrations significantly decreased ($p < 0.05$) in Groups 1 and 2 following administrations of the antifibroid decoction. However, serum total protein concentration significantly increased ($p < 0.05$) in the Depo Provera group compared to the control (Table 1). Serum albumin concentration also increased in the Depo Provera group but decreased following administration of the higher dose of the decoction (Table 1).

Lipid profile analysis revealed that administration of the higher dose of the decoction led to a significant decrease ($p < 0.05$) in serum total cholesterol, low-density lipoprotein cholesterol (LDL-C), and triglycerides compared to the control (Table 2). In the Depo Provera group, LDL-C concentration also decreased significantly ($p < 0.05$) compared to the control. High-density lipoprotein cholesterol (HDL-C) levels remained unchanged ($p > 0.05$) across all groups, including the Depo- Provera group, following treatment.

Plasma glucose concentration increased significantly ($p < 0.05$) in the low-dose decoction and Depo Provera groups compared with the control (Table 3).

Table 1: Effect of varied doses of herbal 'antifibroid' decoction and Depo provera on protein profile in pregnant Dutch white rabbits

Group/ Treatment	Dose (mg/kg)	**Protein Profile**			
		Albumin (g/l)	Globulin (g/l)	Urea (µmol/l)	Total protein (g/l)
Decoction (i)	40.0	31.76±1.66[b]	32.66±0.76[a]*	5.76±1.05[a]*	64.00 ± 2[ab]*
Decoction (ii)	20.0	45 ±10.11*	22.3 ±1.52[a]*	7.33± 0.20	67.00± 2[ab]*
Depo provera	2.73	42 ±1.00[a]*	37.33±0.57*	3.70±0.00[a]*	79.00± 2[a]*
Control	Nil	31.67±1.53[b]	39.33± 0.57	7.83± 0.30[b]	71.00± 1[b]

Values represent Mean ± SD of 5 animals and triplicate determinations
[a]* P (< 0.05) significant difference compared to the negative control
[b]* P (< 0.05) significant difference compared to the positive control
Decoction (i) are Group 1 that received oral administration of 1 mL of 40 mg of the herbal decoction, for 12 consecutive days
Decoction (ii) are Group 2 that received oral administration of 1 mL of 20 mg of the herbal decoction, for 12 consecutive days

Table 2: Effect of varied doses of herbal 'antifibroid' decoction and Depo provera on Lipid profile in pregnant Dutch-white rabbits

		Lipid Profile			
Group/ Treatment	Dose mg/kg	Total Chol.	HDL Chol.	LDL Chol.	Triglyceride
Decoction (i)	40.0	2.80±0.20*[a]	1.18± 0.17	0.90±0.10[ab]*	1.46± 0.15[ab]*
Decoction(ii)	20.0	4.93 ±0.15	1.40 ± 0.1	2.53 ± 0.15	2.10± 0.10[a]*
Depo provera	2.73	5.00 ± 0.10	1.56± 0.15	2.63± 0.05[a]*	1.90± 0.10[a]*
Control	Nil	5.10 ± 0.55	1.26± 0.11	2.30 ± 0.10	2.90 ± 0.05[b]*

Values represent Mean ± SD of 5 animals and triplicate determinations
[a]* P (< 0.05) significant difference compared to the negative control
[b]* P (< 0.05) significant difference compared to the positive control
Key: Chol- Cholesterol, HDL Chol- High density Lipoprotein Cholesterol, LDL- Low density lipoprotein Cholesterol
Decoction (i) are Group 1 that received oral administration of 1 mL of 40 mg of the herbal decoction, for 12 consecutive days
Decoction (ii) are Group 2 that received oral administration of 1 mL of 20 mg of the herbal decoction, for 12 consecutive days

Table 3: Effect of varied doses of herbal 'Antifibroid' decoction on blood fasting sugar in pregnant Dutch-white rabbits

Group/ Treatment	Dose mg/kg	Glucose Mmol/l
Decoction (i)	40.0	3.8 ± 0.20
Decoction (ii)	20.0	5.0 ± 0.00[a]*
Depo provera	2.73	8 ± 0.02[a]*
Control	Nil	4.1 ± 0.1[b]

Values represent Mean ± SD of 5 animals and triplicate determinations
[a]* P (< 0.05) significant difference compared to the negative control
[b]* P (< 0.05) significant difference compared to the positive control
Decoction (i) are Group 1 that received oral administration of 1 mL of 40 mg of the herbal decoction, for 12 consecutive days
Decoction (ii) are Group 2 that received oral administration of 1 mL of 20 mg of the herbal decoction, for 12 consecutive days

DISCUSSION

Lipid profiles are critical markers of metabolic and cardiovascular health, and their modulation during pregnancy may have clinical implications (26,27,28,). In this study, administration of a higher dose of the herbal antifibroid decoction significantly reduced serum cholesterol, LDL cholesterol, and triglycerides without affecting HDL cholesterol. These alterations suggest that the decoction may have influenced hepatic lipid metabolism, possibly through the action of bioactive compounds commonly present in medicinal plants, such as saponins and tannins, which have been reported to exert hypocholesterolemic and antihyperlipidemic effect (29, 30). Interestingly, the observed reduction in LDL and triglycerides contrasts with the typical gestational pattern of hyperlipidemia, particularly in the second and third trimesters (31). Normally, rising estrogen and progesterone levels during pregnancy promote lipogenesis to meet fetal energy demands [35, 36]. Therefore, the decoction's effect may indicate a modulation of lipoprotein synthesis or breakdown pathways. However, in the absence of complementary data such as insulin levels, hepatic enzyme activity, or placental lipid transfer indices, these mechanisms remain speculative.

The Depo Provera group also exhibited a significant reduction in triglycerides, though total cholesterol and LDL levels remained unchanged. This aligns with previous findings that progestin-based contraceptives such as medroxyprogesterone acetate have varied effects on lipid metabolism, with generally minimal cardiovascular risk [32].

With respect to protein metabolism, the increased total protein and albumin observed in the Depo Provera group is consistent with prior studies indicating that exogenous progestins may alter hepatic protein synthesis [33, 34]. Conversely, the significant reduction in serum total protein and globulin observed in the herbal decoction groups may suggest hepatic suppression or altered protein turnover, possibly related to the phytochemical constituents of the decoction. However, due to the absence of hepatic histology, inflammatory markers, or nitrogen balance studies, this interpretation should be considered preliminary.

Glucose levels were elevated in both the low-dose decoction and Depo Provera groups. This could reflect increased maternal gluconeogenesis to support fetal demands, a well-documented physiological adaptation in mid to late pregnancy [35]. However, the fact that glucose levels were higher in the low-dose group and normalized at higher doses may point toward a biphasic dose-dependent metabolic response of the herbal extract. Again, the absence of supporting markers such as serum insulin, HOMA-IR index, or body weight changes limits our ability to explain the exact mechanism of glucose modulation.

Importantly, this study did not assess fetal development, placental weight, or potential teratogenic effects, which are crucial endpoints for evaluating reproductive safety. As such, while the observed maternal metabolic effects are noteworthy, their implications for fetal health and pregnancy outcomes remain unknown. Furthermore, no formal qualitative or quantitative phytochemical profiling of the decoction was performed, and the identity or concentration of active compounds remains uncharacterized. These limitations necessitate cautious interpretation of our findings and highlight the need for more robust follow-up studies.

Limitations and Scope of Study

This study has some limitations that should be acknowledged. First, the serum samples were pooled per group, which narrows the ability to analyze individual variability and reduced the statistical power of the findings. Secondly, while the herbal decoction used in the study was formulated based on traditional practice, no qualitative or quantitative phytochemical profiling was conducted. As such, the identity, potency, and potential interactions of the bioactive constituents remain unknown.

Furthermore, the present study focused solely on maternal metabolic parameters and did not assess fetal outcomes such as viability, weight, placental histology, or teratogenic effects. Without these data, conclusions regarding reproductive safety or risk to fetal development are not possible. Additionally, important metabolic and endocrine markers—such as insulin levels, body weight changes, and hormonal profiles—were not evaluated, limiting mechanistic interpretations of the observed biochemical changes.

These limitations underscore the preliminary nature of the findings and the need for more comprehensive studies incorporating phytochemical analysis, reproductive toxicity assessments, and long-term outcome measures.

Conclusion

This study provides preliminary evidence that a traditional herbal antifibroid decoction can modulate key metabolic parameters—including lipid, protein, and glucose profiles—in pregnant rabbits. While some findings, such as the reduction in LDL and triglycerides, suggest potential cardiovascular benefits, the observed alterations in glucose and protein metabolism warrant further investigation.

The current study was not designed to assess reproductive toxicity or fetal safety, and therefore, no clinical recommendations should be made at this stage**.** Given the lack of data on fetal outcomes, hormonal levels, histopathology, and bioactive compound profiling**,** these findings must be interpreted with caution. Future studies with larger sample sizes**,** detailed phytochemical analyses**,** dose–response designs**,** and inclusion of reproductive and developmental endpoints are essential to fully evaluate the safety and efficacy of such herbal preparations during pregnancy

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Conflict of Interest

None to declare

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