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Pharmacological Evaluation of Capparis Zeylanica Linnplant Extract in Letrozole-Induced PCOS in Rat

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ABSTRACT
Polycystic ovary syndrome (PCOS) is a complex endocrine and metabolic disorder affecting reproductive-age women globally. It is characterized by hyperandrogenism, anovulation, and polycystic ovarian morphology, often accompanied by insulin resistance and systemic inflammation. The current study investigates the therapeutic efficacy of Capparis zeylanica Linn ethanolic extract in a letrozole-induced PCOS rat model. Letrozole was administered orally for 21 days to induce PCOS, followed by treatment with Capparis zeylanica Linn extract at doses of 100 mg/kg and 300 mg/kg. Clomiphene citrate served as the standard comparator. Multiple parameters including body weight, fasting blood glucose, serum testosterone, and physical symptoms (hair loss, vaginal dryness, skin infections) were monitored. Histopathological assessment of ovarian tissue was also performed. The extract at 300 mg/kg significantly reversed PCOS-associated alterations, as evidenced by normalized testosterone and glucose levels, improvement in estrous cyclicity, and restoration of ovarian architecture. Additionally, notable reductions in external symptoms were observed by Day 49. Phytoconstituents in Capparis zeylanica Linn, such as flavonoids, polyphenols, and terpenoids, likely mediated its anti-androgenic, anti-inflammatory, and insulin-sensitizing effects. The extract's efficacy was dose-dependent and comparable to that of clomiphene citrate. Overall, this study highlights the multifactorial efficacy of Capparis zeylanica Linn in managing PCOS and supports its potential as a phototherapeutic alternative to conventional treatments

Keywords: *Polycystic Ovary Syndrome; Capparis zeylanica Linn; Letrozole; Clomiphene Citrate; Phytotherapy; Hormonal Imbalance; PCOS Rat Model; Ovarian Histopathology; Antioxidant; Anti-androgenic*

1.INTRODUCTION

Polycystic ovary syndrome (PCOS) is a chronic, heterogeneous endocrine disorder affecting 8–13% of women of reproductive age globally, with prevalence varying by ethnicity, diagnostic criteria, and geographic region [1]. It is characterized by hyperandrogenism, chronic anovulation, and polycystic ovarian morphology, often accompanied by metabolic disturbances such as insulin resistance, obesity, and dyslipidemia [2]. The syndrome is also associated with a higher risk of infertility, type 2 diabetes mellitus, cardiovascular disease, and endometrial carcinoma [3].

1.1 Etiology and Pathophysiology

The etiology of PCOS is multifactorial and remains incompletely understood. Contributing factors include:

- Genetic predisposition: Family history of PCOS or type 2 diabetes increases susceptibility [2].
- Neuroendocrine dysfunction: Altered gonadotropin-releasing hormone (GnRH) pulsatility leads to increased LH secretion and androgen production [3].
- Insulin resistance: Hyperinsulinemia exacerbates ovarian androgen synthesis and inhibits follicular maturation [2].
- Environmental pollutants: Endocrine-disrupting chemicals (EDCs) may interfere with hormonal regulation [2].
- Gut dysbiosis: Emerging evidence links altered gut microbiota with systemic inflammation and metabolic dysfunction in PCOS [2].

1.2 Risk Factors

Several modifiable and non-modifiable risk factors have been identified:

- Obesity and sedentary lifestyle
- High glycemic index diets
- Early menarche
- Psychosocial stress

- Exposure to endocrine disruptors

These factors contribute to the development of hyperinsulinemia, oxidative stress, and chronic low-grade inflammation, which collectively impair ovarian function and exacerbate PCOS symptoms [2], [3].

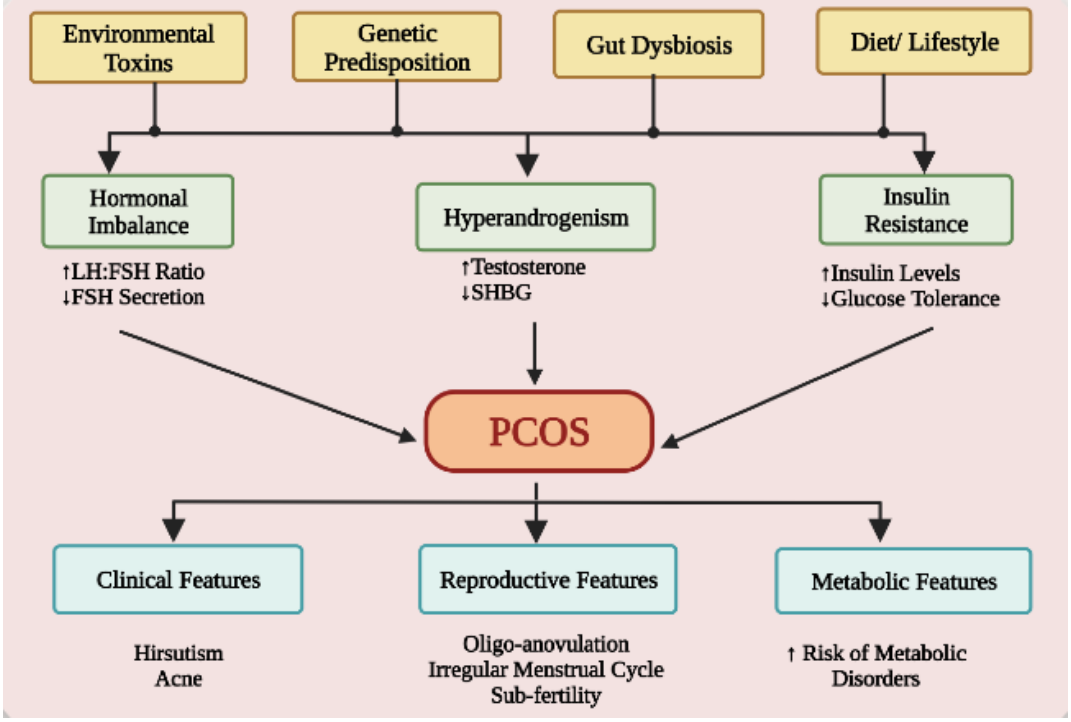


Figure 1 illustrates the multifactorial origins and systemic consequences of PCOS, highlighting how environmental toxins, gut dysbiosis, and genetic predisposition lead to hormonal imbalance and insulin resistance, which in turn drive the clinical phenotype.

2. PLANT PROFILE: Capparis zeylanica Linn

Capparis zeylanica Linn. (Family: Capparaceae), commonly known as Indian caper, is a climbing shrub widely distributed across tropical Asia. Traditionally used in Ayurveda and Siddha medicine, it is known for its anti-inflammatory, antidiabetic, hepatoprotective, and wound-healing properties.[4,5]

2.1 TAXONOMY

Rank	Classification
Kingdom	Plantae
Division	Magnoliophyta (Angiosperms)
Class	Magnoliopsida (Dicotyledons)
Order	Brassicales
Family	Capparaceae
Genus	*Capparis*
Species	*Capparis zeylanica* Linn.

2.2 Vernacular Names

- Hindi: Himsra, Kabra
- Sanskrit: Himsra
- Tamil: Sirukattai
- Telugu: Vankara
- Malayalam: Neer-mulluka

2.3 Habitat and Morphology

This species thrives in dry deciduous forests, scrublands, and rocky terrains. It is a climbing shrub with ovate leaves, thorny stems, and showy white to pink flowers with long stamens. The plant bears globular berries that turn reddish when ripe. Its morphological features support its identification and traditional use in ethnomedicine [6].

Figure 2. Capparis zeylanica Linn flower in full bloom, displaying its characteristic long, filamentous stamens and delicate pink petals. The floral morphology, including prominent reproductive structures, is indicative of its pollination strategy and botanical identity. This species is traditionally used in ethnomedicine and is under investigation for its anti-inflammatory and hormone-modulating properties relevant to PCOS management.

2.4 Phytochemical Composition

Phytochemical screening of Capparis zeylanica Linn has revealed the presence of:

- Flavonoids (e.g., quercetin, kaempferol): Exhibit antioxidant and anti-androgenic effects.
- Terpenoids: Possess anti-inflammatory and immunomodulatory properties.
- Phenolic compounds: Contribute to insulin-sensitizing and free radical scavenging activity [6], [7].

2.5 Pharmacological Relevance in PCOS

Recent studies suggest that plant-based therapies can modulate multiple PCOS-related pathways. Capparis zeylanica Linn, in particular, has shown potential in:

- Reducing serum testosterone levels
- Improving insulin sensitivity
- Restoring ovarian histoarchitecture
- Alleviating physical symptoms such as alopecia and skin infections

These effects are attributed to its ability to counteract oxidative stress, regulate hormonal imbalance, and enhance follicular development [6], [7] .

3. MATERIAL AND METHODS

3.1 Plant Material and Extraction

Fresh Capparis zeylanica Linn leaves were procured from Saharanpur, Uttar Pradesh, and authenticated by the Botanical Survey of India, Dehradun. The leaves were shade-dried, coarsely powdered, and subjected to Soxhlet extraction using ethanol. The solvent was evaporated using a water bath to yield a

semisolid extract, which was stored at 4°C until further use. Doses of 100 mg/kg and 300 mg/kg were selected based on OECD guidelines.[8]

Figure 2. Soxhlet Assembly

3.2 Animals and Experimental Design

Thirty healthy female Wistar rats (150–200 g) were procured and housed under standard laboratory conditions (25 ± 2°C, 12 h light/dark cycle, and 50 ± 10% humidity), with free access to food and water. The animals were acclimatized for one week and randomized into five groups (n = 6):

1. **Normal Control** – Received vehicle only
2. **Disease Control** – Letrozole (1 mg/kg/day, orally) for 21 days
3. **Standard Group** – Letrozole + Clomiphene citrate (1 mg/kg/day)
4. **Treatment Group I** – Letrozole + Capparis zeylanica Linn extract (100 mg/kg/day)
5. **Treatment Group II** – Letrozole + Capparis zeylanica Linn extract (300 mg/kg/day)

PCOS was induced by daily oral administration of letrozole for 21 days. Treatments were continued for 28 days post-induction.

Evaluation Parameters

- **Physical Observations**: Body weight, hair loss, vaginal dryness, and skin infections were recorded at regular intervals.
- **Biochemical Tests**: Blood samples were collected for analysis of fasting glucose and serum testosterone using standard laboratory methods.
- **Histopathology**: Samples were preserved in 10% formalin and subjected to hematoxylin and eosin staining for microscopic evaluation.

Statistical Analysis

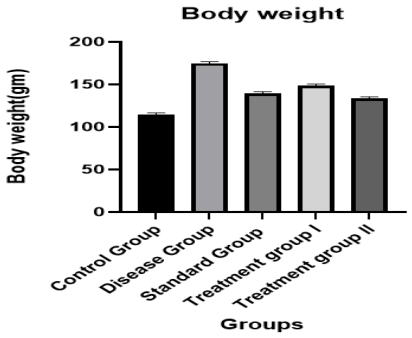
Data were expressed as mean ± standard error of mean (SEM). Statistical comparisons were performed using one-way ANOVA followed by Tukey's post hoc test. P value of $p < 0.05$ was considered statistically significant ($p < 0.01$, $p < 0.001$).

RESULT

I: PHYSICAL EVALUATION

1- BODY WEIGHT:

PCOS induction with letrozole led to a significant increase in body weight compared to the normal group. Treatment with Capparis zeylanica Linn, particularly at 300 mg/kg, attenuated this weight gain, indicating a potential role in metabolic regulation.



Graph no.01: difference in body weight among various groups

2- Vaginal dryness score

Vaginal dryness, a symptom of estrogen deficiency and hormonal imbalance, was markedly elevated in the disease group. Both treatment groups showed a dose-dependent reduction in dryness, with the 300 mg/kg group nearly restoring normal mucosal conditions.

Group	Day 0	Day 21	Day 49
Normal Group	0	0.6	0.2
Disease Group	0	5.0	4.8
Standard Group	0	1.0	0.1
Treatment Group I	0	1.3	0.3
Treatment group II	0	0.7	0

Table 5 shows vaginal dryness score

3- Skin Infection Score (0–5 Scale)

Letrozole-induced PCOS rats exhibited increased skin infections, likely due to hormonal imbalance and immune suppression. Treatment with Capparis zeylanica Linn significantly reduced these symptoms, with the high-dose group showing complete resolution by Day 49.

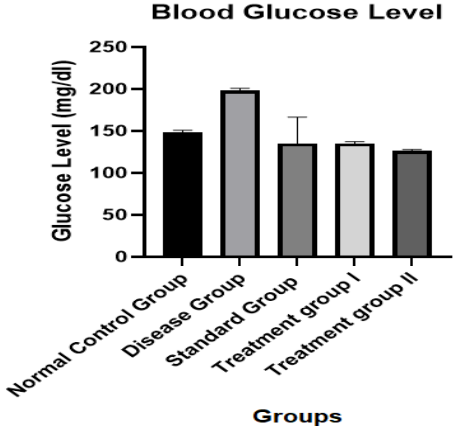
Group	Day 0	Day 21	Day 49
Normal group	0	0	0
Disease group	0	4.8	4.4
Standard group	0	1.2	0.2
Treatment group I	0	1.6	0.5
Treatment group II	0	0.6	0

Table 6 shows skin infection score

II: BIOCHEMICAL PARAMETER

1. BLOOD GLUCOSE LEVEL

Letrozole administration significantly elevated fasting glucose levels, indicating insulin resistance. Treatment with Capparis zeylanica Linn extract, especially at 300 mg/kg, normalized glucose levels, suggesting improved insulin sensitivity.



Graph no.02: Showing the differences in blood glucose level among various group

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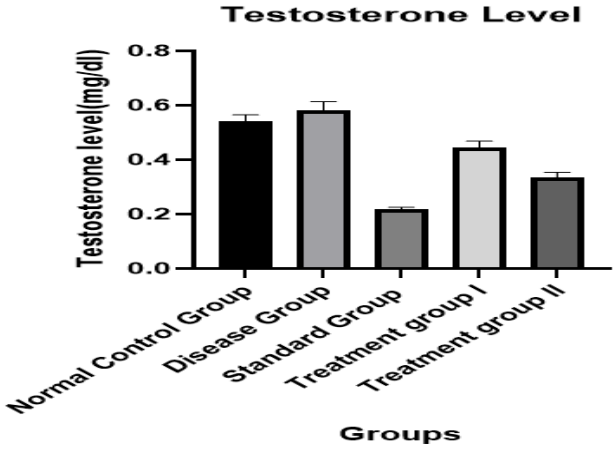
2. BLOOD TESTOSTERONE LEVEL

Hyperandrogenism is a hallmark of PCOS. The disease group showed elevated serum testosterone levels, which were significantly reduced in both treatment groups. The 300 mg/kg dose was nearly as effective as clomiphene citrate in restoring hormonal balance.



Graph no.03: Showing the differences in testosterone level among various group

III: HISTOPATHOLOGICAL CHANGES:

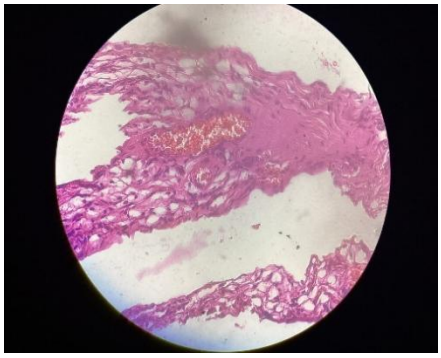


Figure a. Normal group

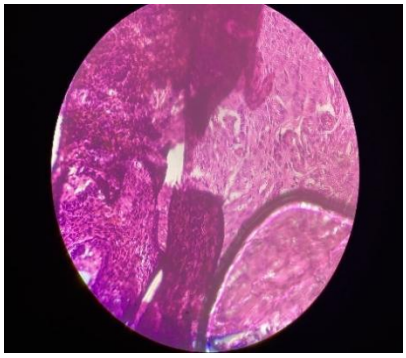


Figure b. Disease group

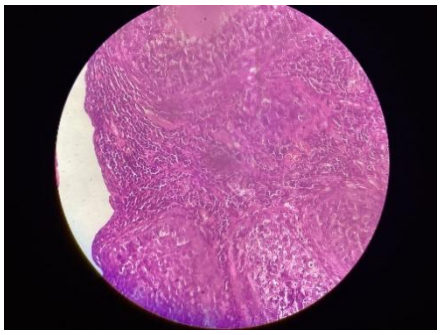


Figure c. Standard group

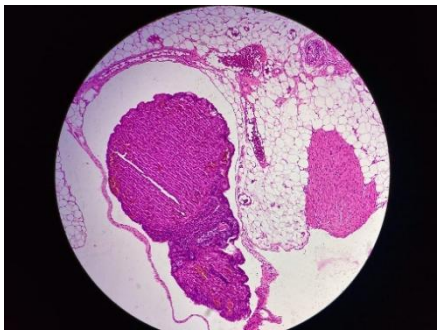


Figure d. Treatment group I

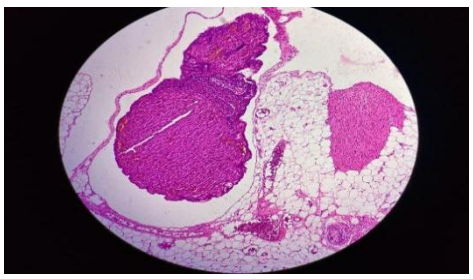


Figure e. Treatment group II

The histological analysis provided crucial insights into ovarian recovery post-treatment. Ovarian sections from the normal control group (Figure a) revealed well-preserved architecture with developing follicles and corpus luteum, indicating regular ovulatory function. The disease control group (Figure b) demonstrated significant cystic degeneration, stromal hyperplasia, and absence of corpus luteum, confirming successful induction of PCOS via letrozole. In contrast, the clomiphene citrate-treated group (Figure c) showed marked improvement in follicular maturation, with partial restoration of the corpus luteum. Treatment Group I (Figure d) (100 mg/kg Capparis zeylanica Linn) displayed moderate architectural recovery, with decreased cystic lesions and emerging healthy follicles. Notably, Treatment Group II (Figure e) (300 mg/kg) showed substantial restoration of follicular development, visible corpus luteum, and reversal of cystic morphology—highlighting dose-dependent therapeutic potential of Capparis zeylanica Linn.

DISCUSSION

The histological analysis provided crucial insights into ovarian recovery post-treatment. Ovarian sections from the normal control group (Figure a) revealed well-preserved architecture with developing follicles and corpus luteum, indicating regular ovulatory function. The disease control group (Figure b) demonstrated significant cystic degeneration, stromal hyperplasia, and absence of corpus luteum, confirming successful induction of PCOS via letrozole. In contrast, the clomiphene citrate-treated group (Figure c) showed marked improvement in follicular maturation, with partial restoration of the corpus luteum. Treatment Group I (Figure d) (100 mg/kg Capparis zeylanica Linn) displayed moderate architectural recovery, with decreased cystic lesions and emerging healthy follicles. Notably, Treatment Group II (Figure e) (300 mg/kg) showed substantial restoration of follicular development, visible corpus luteum, and reversal of cystic morphology—highlighting dose-dependent therapeutic potential of Capparis zeylanica Linn.

CONCLUSION

The findings of this study establish the dose-dependent efficacy of Capparis zeylanica Linn ethanolic extract in reversing the pathophysiological features of letrozole-induced PCOS in rats. The 300 mg/kg dose demonstrated significant improvement in biochemical, histological, and physical parameters—comparable to standard clomiphene citrate treatment. Restoration of ovarian architecture, hormonal balance, glycemic control, and external symptoms like alopecia and mucosal dryness confirm the plant's multifactorial therapeutic potential.

These results position Capparis zeylanica Linn as a promising phytotherapeutic candidate for PCOS management, warranting further exploration of its underlying molecular mechanisms and long-term safety profile.

list of abbreviations

1. PCOS – Polycystic Ovary Syndrome
2. C. zeylanica –Capparis zeylanica Linn
3. LH – Luteinizing Hormone
4. FSH – Follicle Stimulating Hormone
5. SEM – Standard Error of the Mean
6. SD – Standard Deviation
7. H&E – Hematoxylin and Eosin
8. OECD – Organisation for Economic Co-operation and Development
9. ANOVA – Analysis of Variance
10. p.o. – Oral Administration
11. i.p. – Intraperitoneal
12. mg/kg – Milligrams per Kilogram Body Weight
13. EDCs - Endocrine-Disrupting Chemicals
14. GnRH - Gonadotropin-Releasing Hormone
15. BSI - Botanical Survey of India

Conflict of Interest: The author has no conflict of interest.

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Author Contribution

SR- Perform animal experiment and writing original Draft
Draft IT- Original concept
SS- Supervision and critical revision of manuscript

Ethical Approval: The research study was conducted at Siddhartha institute of pharmacy, Near IT park, Dehradun 248001. The animal house is CPCSEA approval. And the registration no. of the animal house – 1435/PO/RE/S/11/CPCSEA.

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