



Evaluation of the Therapeutic Potential of Rheum Emodin Letrozole Induced Polycystic Ovarian Disease in Female Wistar Rats

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ABSTRACT:

Objective: To evaluate the therapeutic potential of Rheum emodi in the management of letrozole induced polycystic ovarian disease (PCOD) in the female Wistar rat model.

Methods: Letrozole (1mg/kg) was administered perorally (p.o) for a period of 21 days for the induction of PCOD, followed by dose of Clomiphene citrate (1mg/kg) with Rheum emodi (100mg/kg, 200mg/kg and 400mg/kg, p.o) for 15 days using 1% CMC as vehicle.

Results: The administration of Letrozole led to abnormal cytochrome serum sex steroid profile, body weight, uterine weight and ovary weight. Rheum emodi was able to successfully exert its protective effect by restoring all the parameters to normal and disappearance of cysts in ovaries.

Conclusion: Rheum emodi showed beneficial effects in Letrozole induced PCOD in female Wistar rats. Its effect was comparable to that of Clomiphene citrate, most widely used treatment for ovulation induction in PCOD condition.

Index Terms: PCOD, Rheum emodi, Letrozole, Clomiphene Citrate, Female Wistar Rats, Hormonal Imbalance.

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I. INTRODUCTION

Polycystic Ovarian Disease (PCOD) is a hormonal and metabolic disorder that predominantly affects women of reproductive age. In recent years, it has increasingly been recognized as a lifestyle-related condition, often linked to sedentary routines, unhealthy dietary patterns, and poor lifestyle practices^[1].

Polycystic Ovarian Disease (PCOD), represents one of the most prevalent and complex endocrinopathies of the female reproductive system. This syndrome has since emerged as a major public health concern globally, affecting an estimated 6–26% of women of reproductive age, with variations attributable to differences in diagnostic criteria, geographical region, and ethnicity^[2]. In South Asian populations, including India, the prevalence has been reported to be particularly high, with some studies indicating rates exceeding 20–22%^[3].

PCOD is defined by a core triad: hyperandrogenism, oligo-anovulation, and polycystic ovarian morphology on ultrasound. However, it presents heterogeneously and is often associated with broader metabolic and endocrine

disturbances such as insulin resistance, hyperinsulinemia, dyslipidaemia, chronic inflammation, elevated AMH, and HPO axis dysfunction. These changes not only affect reproductive health but also increase the long-term risk of conditions like type 2 diabetes, NAFLD, cardiovascular disease, and endometrial cancer^[4].

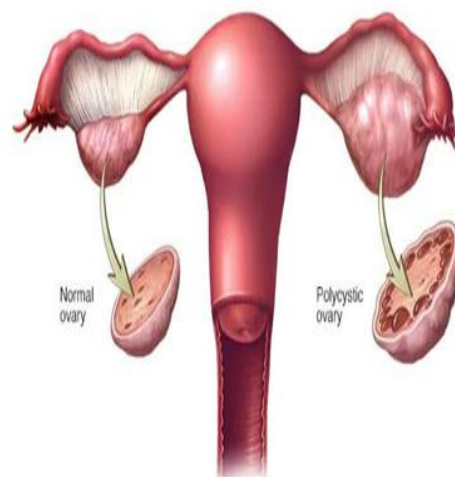




Figure 01: Polycystic ovary shown in the Uterine system^[5]

In a normal menstrual cycle, ovulation occurs when a mature follicle—a fluid-filled cystic structure—reaches a diameter of approximately 18 to 28 mm. The fundamental distinction between healthy ovaries and polycystic ovaries lies in follicle development. Although polycystic ovaries contain multiple small antral follicles, these follicles fail to mature adequately, preventing ovulation. As a result, women with polycystic ovaries experience irregular or absent menstrual cycles. Another common feature of this condition is elevated levels of androgens, particularly testosterone and androstenedione. The excess of these male hormones in the bloodstream often leads to symptoms such as excessive hair growth on the face and body (hirsutism)^[6].

Polycystic Ovarian Disease (PCOD) is a multifaceted endocrine disorder that impacts not only the reproductive system but also metabolic health and overall well-being in women. Several lifestyle-related determinants—including body mass index (BMI), dietary patterns, physical activity, stress levels, and family history—play a critical role in its onset and progression. Evidence suggests that women with elevated BMI are more susceptible to PCOD, as excess adiposity disrupts hormonal balance and intensifies clinical manifestations.

Conversely, regular physical activity has been shown to improve insulin sensitivity, reduce systemic inflammation, and support overall metabolic health, thereby alleviating PCOD-related complications. Nutritional habits are equally important, with both the quality and quantity of food intake influencing symptom management and fertility outcomes. Stress, whether physical or psychological, further contributes to the disorder by altering hormonal regulation and promoting inflammatory responses. Genetic predisposition is another key factor, as a family history of PCOD significantly increases the likelihood of developing the condition.

A holistic understanding of these lifestyle and genetic influences enables healthcare professionals to design individualized treatment strategies. Such personalized management emphasizes the role of lifestyle modifications—including weight regulation, exercise, and dietary control—in improving clinical outcomes and enhancing quality of life. Maintaining a healthy BMI is particularly important, as obesity is strongly

associated with insulin resistance, hyperandrogenism, and a heightened risk of Type 2 diabetes in women with PCOD. Clinically, the disorder may present with hirsutism, acne, irregular menstruation, and reduced fertility. Accurate diagnosis typically involves clinical evaluation alongside investigations such as hormonal assays and ultrasonography. Management strategies focus on addressing immediate health concerns as well as infertility. In overweight women, interventions such as weight reduction, structured exercise programs, dietary modifications, and dermatological care for androgenic symptoms are integral components of therapy^[7].

II. MATERIALS AND METHODS

Experimental animals

All the experimental animals Female Wistar strain (150-250 gm) and housing conditions of animals were maintained as per CCSEA guidelines. Animals were kept in group of six in propylene plastic cages with sterilized husk as bedding material. Animals were provided standard feeding pellets and water ad libitum temperature was maintained at $22 \pm 2^\circ\text{C}$, with light and dark cycle of 12;12 hrs. The animals were transferred to the laboratory at least 1 hour before experiment for proper acclimatization. Animals were acclimatized to the experimental conditions for a period of one week before actual experimentation. The care and handling of animal were in accordance with laboratory with the internationally accepted standard guidelines for animal (CCSEA) permission and approval for animal studies obtained from the Institutional Animal Ethics committee (IAEC).

Preparation of Plant Extract:

In order to determine the best solvent for extraction for the DHAQs solvents like petroleum ether, chloroform, ethyl acetate and ethanol were employed for extraction. 0.5 g of the powdered drug was extracted with the solvent (sample to solvent ratio - 1:50), shaken vigorously for 15 min and left undisturbed for 24 h. The extract obtained was centrifuged at 3000 rpm for 5 min and 1 ml of the supernatant was diluted with methanol (1:100). The same procedure was used for the acid hydrolyzed samples to select the solvent for extracting the enriched quantity of DHAQs generated by acid hydrolysis.

Drugs and reagents



Rheum emodi roots was collected from forest region of Amravati dist. Maharashtra (India). Authentication was done at Department of Botany, Vidyabharati Mahavidyalaya, Camp Road, Amravati and prepared the plant extract. Letrozole was obtained from medical store Amravati. Clomiphene citrate 50 mg tablet manufactured in India by Maneesh Pharmaceuticals Ltd. and brought from pharmacy store Amravati.

Preparation of doses and treatments

The activity of ethanolic extract of Rheum emodi roots as a antioxidant and anti-inflammatory activity of plant using Letrozole-induced PCOD in female wistar rats. Subsequently, Letrozole was administered orally at a dose of 1 mg/kg with CMC 1% as a vehicle. The ethanolic extract of Rheum emodi roots was administered at doses of 100, 200 and 400 mg/kg, which were selected based on a previous acute oral toxicity study. Letrozole, Clomiphene citrate and extract was administered to animals by gavage.

Induction of PCOD in female wistar rats

All the experimental animals except control group, were orally administered with Letrozole (1mg/kg) dissolved in 1 % Carboxy Methyl Cellulose (CMC) once daily for 21 days to induce PCOD condition. The changes in body weight were reported to be the early markers for the induction of PCOD in experimental animals.

Acute toxicity studies

The acute toxicity of prepared extract was already performed using OECD 452 guidelines.

Experimental design

Rats were divided into six groups with six animals each. The first group receive oral normal saline, the second group receives Letrozole 1 mg/kg orally 1ml. Third group received Clomiphene citrate (1 mg/kg), fourth, fifth and sixth group receives oral dose of (100 mg/kg, 200 mg/kg and 400 mg/kg respectively). The rats were randomly divided into 6 groups of 6 rats each.

Group I: Normal Control group which receives saline solution.

Group II: Negative control served as the PCOD group which received letrozole (1mg/kg).

Group III: Standard Group in this group were administered Clomiphene citrate a dose of 1mg/kg body weight orally for 15 days.

Group IV: Animals were administered ethanolic extract of Rheum emodi roots at a dose of 100 mg/kg body weight orally for 15 days.

Group V: Animals were administered ethanolic extract of Rheum emodi roots at a dose of 200 mg/kg body weight orally for 15 days.

Group VI: Animals were administered ethanolic extract of Rheum emodi roots at a dose of 400 mg/kg body weight orally for 15 days.

Blood Sample Collection and Biochemical Analysis

- **Blood Collection:** After the induction period, 1 ml of blood was collected from each animal via [tail vein puncture].
- **Biochemical Analysis:** Serum was separated and hormones parameters such as luteinizing hormone (LH), follicle stimulating hormone (FSH), estrogen and testosterone were estimated using standard biochemical process

Post-Treatment Biochemical Analysis and organ collection:

At the end of the treatment period, Blood samples were collected from the carotid arteries and centrifuged at 3000 rpm for 10 min under cool temperature (4°C) to separate the plasma, and the biochemical parameters (LH, FSH, Estrogen and Testosterone) were measured and recorded for all groups to observe changes. Animals were humanely sacrificed using diluted diethyl ether (2 ml/kg) as an anesthetic. Ovaries and Uterus were carefully excised and fixed in 10% neutral buffered formalin for examination.

Organs removed

• Collection of materials

Both ovaries and Uterus was collected from animals, organs showing gross morbid changes along with normal sample. The ovaries and uterus are identified, dissected carefully using sterile surgical scissors and forceps, and separated from surrounding adipose tissues without causing damage to the organs. The connective tissues and blood clots are gently removed using normal saline.

• Washing of Organs

The isolated ovaries and uterus are washed immediately with chilled normal saline (0.9% NaCl) to remove blood and tissue debris. Excess



saline is removed gently using filter paper or blotting paper.

After weighing, the organs are transferred immediately into labelled specimen containers containing 10% Neutral Buffered Formalin (NBF). The organs are fixed for 24–48 hours at room temperature to preserve cellular architecture and prevent autolysis.

Statistical Analysis.

All values are expressed as mean \pm SEM. The statistical differences among different groups were analyzed using one-way of analysis of variance (ANOVA), for determining the significant difference. The intergroup significance was analyzed using Tukey's test. The difference was considered significant if $p < 0.05$, moderately significant if $p < 0.01$, and highly significant if $p < 0.001$.

III. RESULTS

Evaluation Parameters:

1. Effect of ethanolic extract of root of Rheum emodi on Uterus weight:

The effect of letrozole, standard drug treatment, and ethanolic extract of Rheum emodi on uterine weight in female Wistar rats. The negative control group showed a significant ($p < 0.0001$) decrease in uterine weight when compared with the normal control group, confirming the successful induction of PCOD. Treatment with Clomiphene citrate (1 mg/kg) and the extract-treated groups, Rheum emodi at doses of 100 mg/kg, 200 mg/kg, and 400 mg/kg also showed significantly ($p < 0.0001$) increase uterine weight compared to the negative group.

Table 01: Effect of ethanolic extract of root of Rheum emodi against letrozole- induced polycystic ovarian disease-related parameters in rats (Uterine weight)

Group	Treatment (n=6)	Uterine weight (g)
Control	Normal control	123.6 \pm 1.1
Negative control	Letrozole	73.8 \pm 1.01
Standard	Clomiphene citrate	104.6 \pm 0.8
Treatment I	Rheum emodi (100 mg/kg)	92.6 \pm 0.8
Treatment II	Rheum emodi (200 mg/kg)	98.6 \pm 0.8
Treatment III	Rheum emodi (400 mg/kg)	99.5 \pm 0.4

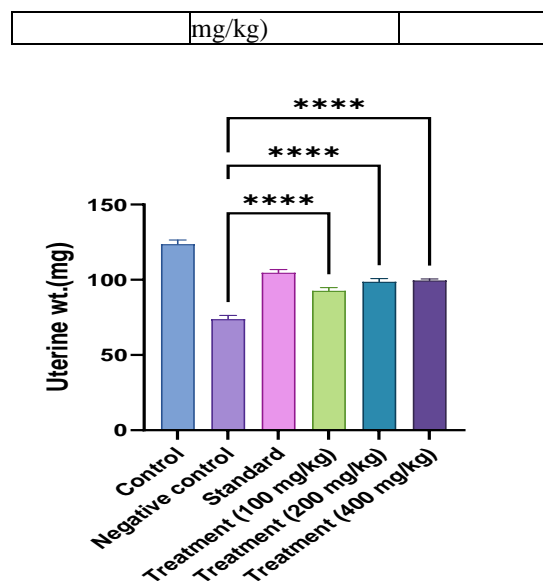


Figure 02: Effect of Letrozole (1 mg/kg), Ethanolic extract of Rheum emodi roots (100 mg/kg, 200 mg/kg, 400 mg/kg) and Clomiphene citrate (1 mg/kg) on uterine weight. All values are mean \pm SEM (n = 6). Statistical comparisons between each treatment and Letrozole induced Polycystic ovaries in rats analyzed by one way ANOVA followed by Tukey's multiple comparison test significant at $p^{****} < 0.0001$ vs Letrozole group.

2. Effect of ethanolic extract of root of Rheum emodi on Ovarian weight :

The effect of letrozole, standard drug treatment, and ethanolic extract of Rheum emodi on ovary weight in female Wistar rats. The negative control group showed a significant ($p < 0.0001$) increase in ovary weight compared to the normal control group, confirming the induction of PCOD. Treatment with Clomiphene citrate (1 mg/kg) reduced the ovary weight towards normal values. Similarly, treatment with ethanolic extract of Rheum emodi at doses of 100 mg/kg, 200 mg/kg, and 400 mg/kg also showed significant ($p < 0.0001$) reduction in ovary weight compared to the induced group.



Table 02: Effect of ethanolic extract of root of Rheum emodi against letrozole- induced polycystic ovarian disease-related parameters in rats (Ovary weight)

Group	Treatment (n=6)	Ovary weight (g)
Control	Normal control	31.50±0.4
Negative control	Letrozole	65.50±0.7
Standard	Clomiphene citrate	47.33±0.4
Treatment I	Rheum emodi (100 mg/kg)	57.0±0.5
Treatment II	Rheum emodi (200 mg/kg)	52.3±0.8
Treatment III	Rheum emodi (400 mg/kg)	51.0±0.3

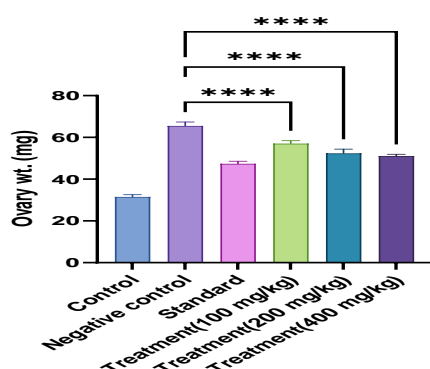


Figure 03: Effect of Letrozole (1 mg/kg), Ethanolic extract of Rheum emodi roots (100 mg/kg, 200 mg/kg, 400 mg/kg) and Clomiphene citrate (1 mg/kg) on ovary weight. All values are mean ± SEM (n = 6). Statistical comparisons between each treatment and Letrozole induced Polycystic ovaries in rats analyzed by one way ANOVA followed by Tukey's multiple comparison test significant at $p^{****} < 0.0001$ vs Letrozole group.

3. Effect of ethanolic extract of root of Rheum emodi on LH, FSH, Estrogen and Testosterone:

The hormonal analysis showed significant alterations in serum hormone levels in the letrozole-induced PCOD group when compared with the normal control group. The negative control group significant ($p < 0.0001$) increase in LH and testosterone levels along with a reduction in FSH and estrogen levels, indicating hormonal imbalance associated with PCOD. Treatment with Clomiphene citrate (1 mg/kg) significantly restored these altered hormone levels towards normal values. The administration of ethanolic extract of Rheum emodi at doses of 100 mg/kg, 200 mg/kg, and 400 mg/kg showed significantly ($p < 0.0001$) improvement in hormonal balance by decreasing elevated LH and testosterone levels while increasing FSH and estrogen levels as compared to the negative control group.

Table 03: Effect of ethanolic extract of root of Rheum emodi against letrozole- induced polycystic ovarian disease-related hormonal parameters in rats (LH, FSH, Estrogen, Testosterone)

Group	Treatment (n=6)	LH (ng/ml)	FSH (ng/ml)	Estrogen (pg/mL)	Testosterone (ng/ml)
Control	Normal control	5.21±0.06	9.75±0.07	64.16±1.16	34.50±0.4
Negative control	Letrozole	12.06±0.08	4.35±0.07	23.0±1.06	82.66±0.8
Standard	Clomiphene citrate	6.66±0.06	7.9±0.07	47.50±0.7	49.50±0.7
Treatment I	Rheum emodi (100 mg/kg)	10.03±0.20	5.65±0.07	28.66±0.7	73.66±0.8
Treatment II	Rheum emodi (200 mg/kg)	8.88±0.10	6.917±0.14	37.33±0.8	63.33±0.9
Treatment III	Rheum emodi (400 mg/kg)	7.56±0.08	7.28±0.12	43.16±1.01	53.50±0.7

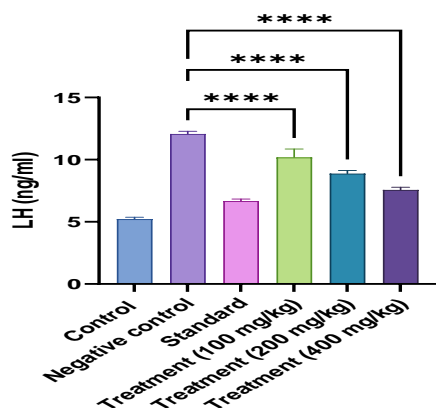


Figure 04: Effect of Letrozole (1 mg/kg), Ethanolic extract of *Rheum emodi* roots (100 mg/kg, 200 mg/kg, 400 mg/kg) and Clomiphene citrate (1 mg/kg) on LH level. All values are mean \pm SEM (n = 6). Statistical comparisons between each treatment and Letrozole induced Polycystic ovaries in rats analyzed by one way ANOVA followed by Tukey's multiple comparison test significant at $p^{****} < 0.0001$ vs Letrozole group.

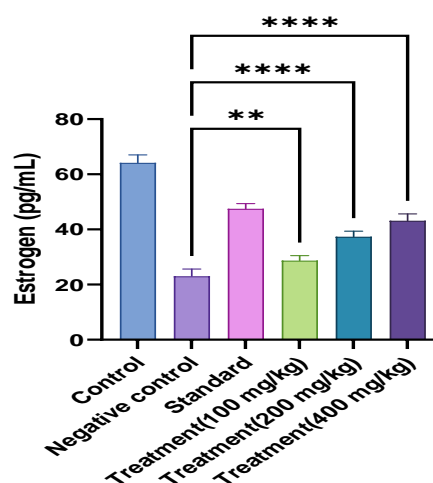


Figure 06: Effect of Letrozole (1 mg/kg), Ethanolic extract of *Rheum emodi* roots (100 mg/kg, 200 mg/kg, 400 mg/kg) and Clomiphene citrate (1 mg/kg) on Estrogen level. All values are mean \pm SEM (n = 6). Statistical comparisons between each treatment and Letrozole induced Polycystic ovaries in rats analyzed by one way ANOVA followed by Tukey's multiple comparison test significant at $p^{****} < 0.0001$ vs Letrozole group.

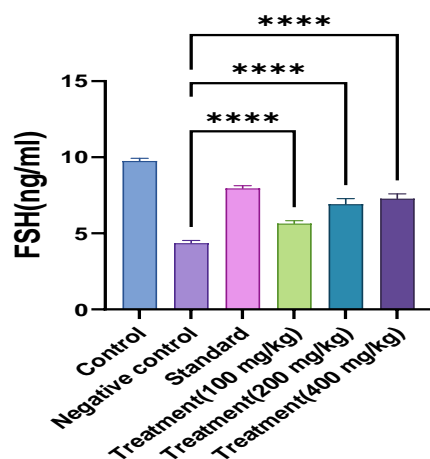


Figure 05: Effect of Letrozole (1 mg/kg), Ethanolic extract of *Rheum emodi* roots (100 mg/kg, 200 mg/kg, 400 mg/kg) and Clomiphene citrate (1 mg/kg) on FSH level. All values are mean \pm SEM (n = 6). Statistical comparisons between each treatment and Letrozole induced Polycystic ovaries in rats analyzed by one way ANOVA followed by Tukey's multiple comparison test significant at $p^{****} < 0.0001$ vs Letrozole group.

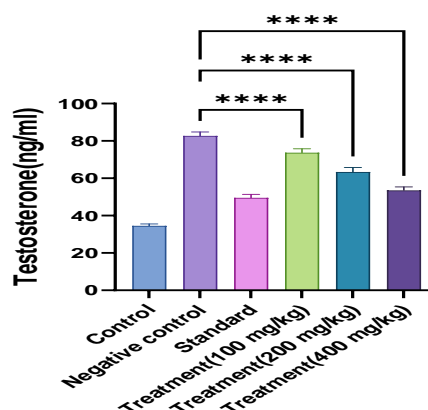


Figure 07: Effect of Letrozole (1 mg/kg), Ethanolic extract of *Rheum emodi* roots (100 mg/kg, 200 mg/kg, 400 mg/kg) and Clomiphene citrate (1 mg/kg) on Testosterone level. All values are mean \pm SEM (n = 6). Statistical comparisons between each treatment and Letrozole induced Polycystic ovaries in rats analyzed by one way ANOVA followed by Tukey's multiple comparison test significant at $p^{****} < 0.0001$ vs Letrozole group.



4. Effect of ethanolic extract of root of *Rheum emodi* on Body weight.

The negative control group showed a significant ($p < 0.0001$) increase in body weight compared to the normal control group, indicating metabolic alterations associated with PCOD. Treatment with Clomiphene citrate (1 mg/kg) significantly reduced and, treatment with ethanolic extract of *Rheum emodi* at doses of 100 mg/kg, 200 mg/kg, and 400 mg/kg also showed significant ($p < 0.0001$) reducing body weight compared to the letrozole group.

Group	Treatment (n=6)	Body weight (gm)
Control	Normal control	206.5±0.4
Negative control	Letrozole	274.16±1.07
Standard	Clomiphene citrate	209.67±0.8
Treatment I	<i>Rheum emodi</i> (100 mg/kg)	227.67±0.8
Treatment II	<i>Rheum emodi</i> (200 mg/kg)	218.67±0.8
Treatment III	<i>Rheum emodi</i> (400 mg/kg)	213.67±0.8

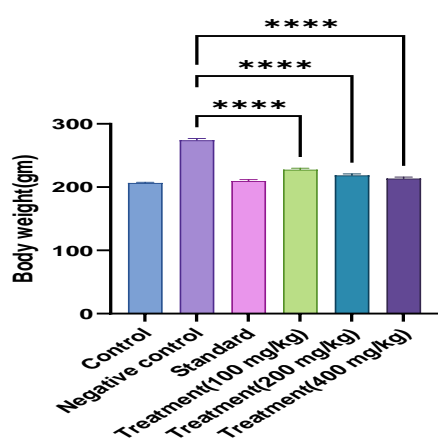


Figure 08: Effect of Letrozole (1 mg/kg), Ethanolic extract of *Rheum emodi* (100 mg/kg, 200 mg/kg, 400 mg/kg) and Clomiphene citrate (1 mg/kg) on Body Weight. All values are mean \pm SEM (n = 6). Statistical comparisons between each treatment and Letrozole induced Polycystic ovaries in rats analyzed by one way ANOVA followed by Tukey's multiple comparison test significant at $p^{****} < 0.0001$ vs Letrozole group.

IV. DISCUSSION

Polycystic Ovarian Disease (PCOD) is one of the most common endocrine and metabolic disorders affecting women of reproductive age. The disorder is characterized by hormonal imbalance, irregular ovulation, hyperandrogenism, ovarian cyst formation, menstrual irregularities, infertility, obesity, and metabolic disturbances. In recent years, the prevalence of PCOD has increased considerably due to changes in lifestyle, stress, dietary habits, and sedentary behavior. Although several synthetic drugs are available for the management of PCOD, long-term therapy is often associated with adverse effects and incomplete therapeutic outcomes. Therefore, there is an increasing need to explore plant-based therapies possessing better safety profiles and multi-targeted therapeutic actions.

The present study was undertaken to evaluate the therapeutic potential of ethanolic extract of *Rheum emodi* roots against letrozole-induced polycystic ovarian disease in female Wistar rats. Letrozole is a non-steroidal aromatase inhibitor that suppresses the conversion of androgens into estrogens, thereby producing hyperandrogenism, anovulation, cystic ovarian morphology, and endocrine abnormalities similar to human PCOD. Hence, the letrozole-induced rat model is considered a reliable and widely accepted experimental model for studying PCOD. In the present investigation, administration of letrozole successfully induced PCOD in female Wistar rats, as evidenced by increased body weight, altered ovarian and uterine weight, elevated testosterone and luteinizing hormone (LH) levels, decreased follicle stimulating hormone (FSH) and estrogen levels, along with some other alterations in ovaries. These findings are in accordance with previously reported studies demonstrating that letrozole induces endocrine and metabolic disturbances associated with PCOD.

Phytochemical screening of the ethanolic extract of *Rheum emodi* roots revealed the presence of several important bioactive constituents such as anthraquinones, flavonoids, tannins, phenolic compounds, glycosides, alkaloids, saponins, and steroids. These phytoconstituents are known to possess antioxidant, anti-inflammatory, antihyperlipidemic, hormonal balancing, and insulin-sensitizing properties, which may contribute to the therapeutic effects observed in the present study. Body weight is considered one of the important indicators in experimental PCOD studies



because obesity and abnormal weight gain are strongly associated with hormonal imbalance and insulin resistance. In the present study, letrozole-treated animals showed a significant increase in body weight when compared with the normal control group. This increase may be attributed to hormonal imbalance, androgen excess, altered lipid metabolism, and insulin resistance induced by letrozole administration. Treatment with ethanolic extract of *Rheum emodi* roots at doses of 100 mg/kg, 200 mg/kg, and 400 mg/kg significantly reduced body weight when compared with the disease control group. Among all treatment groups, the higher dose showed more pronounced activity, which was comparable with the standard drug clomiphene citrate. The reduction in body weight may be due to the presence of phenolic compounds that improve metabolic function and reduce oxidative stress.

The ovary and uterus are highly sensitive reproductive organs affected during PCOD. In the present study, letrozole administration altered ovarian and uterine weights due to follicular cyst formation, hormonal imbalance, and disrupted folliculogenesis. Increased ovarian weight in the disease control group may be associated with the development of multiple cystic follicles and stromal hypertrophy, whereas reduction in uterine weight may be due to suppression of estrogen synthesis caused by aromatase inhibition. Treatment with *Rheum emodi* extract significantly normalized ovarian and uterine weights in a dose-dependent manner. The improvement in ovarian weight suggests restoration of normal follicular development and reduction in cyst formation. Similarly, normalization of uterine weight indicates improvement in estrogenic activity and restoration of reproductive function. These findings suggest that *Rheum emodi* may exert protective effects on reproductive tissues by modulating endocrine imbalance. Hormonal imbalance is one of the hallmark features of PCOD. In the present study, the negative control group showed elevated serum testosterone and LH levels along with reduced FSH and estrogen levels. Increased LH secretion stimulates ovarian theca cells to produce excessive androgens, leading to follicular arrest and cyst formation. Reduced FSH levels impair normal follicular maturation and ovulation. Decreased estrogen levels are mainly due to inhibition of aromatase activity by letrozole. Administration of ethanolic extract of *Rheum emodi* roots significantly restored altered hormonal

parameters toward normal levels. Treatment reduced elevated testosterone and LH levels while increasing FSH and estrogen levels. The effect was more prominent at higher doses and was comparable with clomiphene citrate treatment. The normalization of reproductive hormones may be attributed to phytoconstituents present in *Rheum emodi*, especially flavonoids and anthraquinones, which may influence steroidogenesis, regulate hypothalamic-pituitary-ovarian axis activity, and improve ovarian function. Clomiphene citrate, used as the standard drug in the present study, acts as a selective estrogen receptor modulator and stimulates ovulation by increasing gonadotropin secretion. The standard treated group showed significant improvement in hormonal profile and reproductive parameters, confirming the validity of the experimental model. Interestingly, the higher doses of *Rheum emodi* extract demonstrated effects approaching those of the standard drug, indicating its potential therapeutic usefulness. The higher dose demonstrated near-normal ovarian architecture, indicating significant protective and restorative activity against letrozole-induced ovarian damage. The beneficial effects observed in the present study may be associated with the antioxidant and anti-inflammatory activities of *Rheum emodi*. Oxidative stress is considered an important contributing factor in the pathogenesis of PCOD. Excess reactive oxygen species can impair ovarian steroidogenesis, follicular development, and insulin signaling pathways. Bioactive compounds such as emodin, rhein, chrysophanol, and flavonoids present in *Rheum emodi* are reported to possess potent antioxidant properties capable of reducing oxidative stress and improving reproductive function. Previous studies have reported that *Rheum emodi* possesses anti-inflammatory, antioxidant, hepatoprotective, antidiabetic, and hormonal regulatory activities. These pharmacological properties may collectively contribute to its therapeutic effect against PCOD. The findings of the present study are also supported by earlier investigations on medicinal plants demonstrating beneficial effects in letrozole-induced PCOD models. Overall, the results of the present investigation demonstrate that ethanolic extract of *Rheum emodi* roots possesses significant protective and therapeutic effects against letrozole-induced polycystic ovarian disease in female wistar rats. The extract effectively improved hormonal imbalance, normalized reproductive organ weights, reduced



body weight, and restored ovaries. Among the tested doses, 400 mg/kg exhibited the most significant activity and produced results comparable to the standard drug clomiphene citrate. The study suggests that *Rheum emodi* may serve as a promising natural therapeutic agent for the management of PCOD. However, further studies are required to isolate and characterize the active phytoconstituents responsible for its pharmacological effects. Detailed molecular studies and clinical investigations are also necessary to establish its exact mechanism of action, safety, efficacy, and potential therapeutic application in humans.

V. CONCLUSION

The present study investigate the protective effect of ethanolic extract of *Rheum emodi* roots against experimentally induced PCOD. Letrozole administration successfully induced polycystic ovarian disease in female wistar rats, as evidenced by increased body weight, altered ovarian and uterine weights, elevated testosterone and luteinizing hormone levels, reduced follicle stimulating hormone and estrogen levels. Phytochemical screening confirmed the presence of important bioactive constituents such as flavonoids, anthraquinones, tannins, alkaloids, phenolic compounds, glycosides, and saponins in the ethanolic extract of *Rheum emodi* roots. These phytoconstituents may be responsible for the observed pharmacological activities. Treatment with ethanolic extract of *Rheum emodi* roots significantly improved the altered biochemical, hormonal, and other parameters in letrozole-induced PCOD rats. The extract effectively reduced body weight, normalized ovarian and uterine weights, decreased elevated testosterone and LH levels, and increased FSH and estrogen levels toward normal values. Among all the tested doses, the 400 mg/kg dose showed the most significant therapeutic activity and its effects were found to be comparable with the standard drug.

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