



**INTERNATIONAL JOURNAL OF
PHARMACEUTICAL SCIENCES**
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: <https://www.ijpsjournal.com>



Research Article

Phytochemical and Pharmacological Evaluation of *Coccinia grandis* Leaf Extract on Letrozole-Induced Polycystic Ovary Syndrome in Female Rats

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ARTICLE INFO

Published: 13 Oct 2026

Keywords:

Coccinia grandis; polycystic ovary syndrome; letrozole; metformin; reproductive hormones; oxidative stress; flavonoids; phenolics; female rats.

DOI:

10.5281/zenodo.23332424

ABSTRACT

Background: Polycystic ovary syndrome (PCOS) is a complex endocrine and metabolic disorder characterized by hyperandrogenism, ovulatory dysfunction, hormonal imbalance, insulin resistance, oxidative stress, and associated metabolic abnormalities. The limitations associated with long-term conventional management have stimulated interest in medicinal plants with multiple pharmacological properties. *Coccinia grandis* is a traditionally used medicinal plant with reported hypoglycemic, antioxidant, anti-inflammatory, and metabolic activities. The present study was designed to evaluate the phytochemical composition and pharmacological effects of ethanolic leaf extract of *Coccinia grandis* (ECG) in a letrozole-induced PCOS rat model. Fresh leaves of *Coccinia grandis* were collected, authenticated, shade-dried, powdered, and extracted using 95% ethanol by Soxhlet extraction. Preliminary phytochemical screening and estimation of total flavonoid content (TFC) and total phenolic content (TPC) were performed. Female Wistar albino rats were used for the experimental study. PCOS was induced by oral administration of letrozole (1 mg/kg) in 0.5% carboxymethylcellulose for 21 days. Animals were subsequently treated with metformin (70 mg/kg), ECG 200 mg/kg, or ECG 400 mg/kg for 15 days. Body weight, reproductive organ weights, reproductive hormones, lipid profile, blood glucose, antioxidant parameters, and ovarian histopathology were evaluated. **Results:** Letrozole administration produced characteristic PCOS-associated alterations, including increased body and ovarian weight, reduced uterine weight, elevated testosterone and luteinizing hormone (LH), reduced progesterone, estradiol and follicle-stimulating hormone (FSH), dyslipidemia, increased blood glucose, and reduced glutathione and catalase levels. The 400 mg/kg dose generally produced greater improvement than 200 mg/kg and showed effects approaching those of metformin. Histopathological examination demonstrated marked reduction in cystic follicles and restoration of developing follicles and corpus luteum,

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Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.



particularly in the ECG 400 mg/kg group. Conclusion: The findings suggest that ethanolic leaf extract of *Coccinia grandis* possesses promising reproductive and metabolic protective effects in letrozole-induced PCOS in female rats. The higher dose of 400 mg/kg showed the most pronounced activity among the tested extract doses.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is a heterogeneous endocrine disorder characterized by reproductive, hormonal, and metabolic abnormalities. Disturbances in luteinizing hormone (LH), follicle-stimulating hormone (FSH), estrogen, and testosterone may interfere with normal follicular development and ovulation. Insulin resistance, hyperandrogenism, obesity, oxidative stress, and dysregulation of the hypothalamic-pituitary-ovarian axis are important components of PCOS pathophysiology.

The metabolic consequences of PCOS may include impaired glucose tolerance, dyslipidemia, obesity, and increased long-term cardiometabolic risk. Reproductive manifestations include irregular menstrual cycles, anovulation, follicular arrest, and infertility. Conventional pharmacological management includes insulin sensitizers such as metformin, hormonal therapies, anti-androgenic agents, and ovulation-inducing drugs. Although these therapies can be effective, prolonged treatment and adverse effects may limit their use in some patients.

Medicinal plants have attracted considerable attention as potential complementary approaches because of their diverse phytochemical constituents and multiple biological activities. *Coccinia grandis* belongs to the family Cucurbitaceae and is traditionally used for several metabolic and inflammatory conditions. Different parts of the plant have been reported to possess hypoglycemic, antioxidant, anti-inflammatory,

hypolipidemic, hepatoprotective, and other pharmacological activities.

The thesis literature review reports the presence of several phytochemical classes in *Coccinia grandis*, including alkaloids, flavonoids, steroids, phenolic compounds, glycosides, terpenoids, and other constituents. The plant has also been investigated for antidiabetic and antioxidant effects, providing a rationale for evaluating its possible activity against the metabolic and reproductive abnormalities associated with PCOS.

Letrozole, a non-steroidal aromatase inhibitor, is commonly employed to establish experimental PCOS because inhibition of aromatase decreases estrogen synthesis and produces a hyperandrogenic state. Chronic administration results in endocrine, metabolic, and ovarian morphological alterations resembling several important features of PCOS.

Therefore, the present investigation was undertaken to evaluate the phytochemical characteristics and pharmacological effects of ethanolic leaf extract of *Coccinia grandis* in a letrozole-induced PCOS model in female rats.

2. MATERIALS AND METHODS

2.1 Collection and Authentication of Plant Material

Fresh leaves of *Coccinia grandis* were collected from a local vendor and authenticated by a qualified botanist. The collected leaves were washed, shade-dried, powdered, and used for extraction.

2.2 Preparation of Ethanolic Extract

The powdered leaves were subjected to Soxhlet extraction using 95% ethanol as the extraction solvent. Following extraction, the solvent was



evaporated using a water bath maintained at 45–50°C. The concentrated extract was subsequently air-dried at room temperature. The percentage yield was determined relative to the initial quantity of powdered plant material.

The experimental results reported a practical extract yield of 4.73 g with an overall yield of 8.5% w/w.

2.3 Preliminary Phytochemical Screening

The ethanolic extract was subjected to qualitative phytochemical screening using standard chemical tests. The extract was found to contain alkaloids, flavonoids, steroids, phenolic compounds, cardiac glycosides, and tannins.

2.4 Estimation of Total Flavonoid Content

Total flavonoid content was determined using the aluminium chloride colorimetric method, with quercetin used as the reference standard. The calibration curve showed the regression equation:

$$Y = 0.0057X - 0.0065$$

with $R^2 = 0.9903$.

The total flavonoid content of the extract was reported as 27.65 mg QE/g of extract.

2.5 Estimation of Total Phenolic Content

Total phenolic content was estimated using the Folin–Ciocalteu method with gallic acid as the reference standard. The calibration curve was represented by:

$$Y = 0.0077X + 0.1358$$

with $R^2 = 0.9914$.

The reported total phenolic content was 27.94 µg GAE/g of extract.

2.6 Experimental Animals

Female Wistar albino rats were used. Animals were maintained under controlled environmental conditions with a temperature of $22 \pm 2^\circ\text{C}$, relative humidity of $50 \pm 10\%$, and a 12-h light/dark cycle. Animals were provided food and water ad libitum and acclimatized for at least one week before experimentation.

2.7 Induction of PCOS

PCOS was induced using letrozole at a dose of 1 mg/kg body weight, dissolved in 0.5% carboxymethylcellulose (CMC) and administered for 21 days.

Letrozole inhibits aromatase-mediated conversion of androgens to estrogens, resulting in increased androgenic activity and disruption of normal ovarian function.

2.8 Experimental Design

The study was conducted over a total period of 36 days. The experimental groups consisted of five groups:

Group	Treatment
Normal control	Saline, p.o.
Disease control	Letrozole 1 mg/kg for 21 days
Standard control	Metformin 70 mg/kg for 15 days after induction
ECG 200 mg/kg	<i>C. grandis</i> extract 200 mg/kg for 15 days after induction
ECG 400 mg/kg	<i>C. grandis</i> extract 400 mg/kg for 15 days after induction

The thesis reports six animals per group for the statistical analyses.

2.9 Evaluation Parameters

The following parameters were evaluated: Body weight, Ovarian weight, Uterine weight, Testosterone, Progesterone, Estradiol, FSH, LH,



HDL, Triglycerides, Total cholesterol, Blood glucose, Reduced glutathione (GSH), Catalase (CAT).

2.12 Statistical Analysis

Values were expressed as mean $\pm$ SEM. Statistical analysis was performed using one-way analysis of variance (ANOVA) followed by Bonferroni post hoc test. Statistical significance was considered at $p < 0.05$. The thesis used the following notation:

- * $p < 0.05$
- ** $p < 0.01$
- *** $p < 0.001$

Comparisons were made against the disease-control group.

3. RESULTS

3.1 Phytochemical Screening

Qualitative phytochemical screening of the ethanolic leaf extract demonstrated the presence of alkaloids, flavonoids, steroids, phenols, cardiac glycosides, and tannins.

These findings indicate that the extract contains several classes of bioactive constituents that may contribute collectively to its observed pharmacological effects.

3.2 Total Flavonoid and Phenolic Content

The total flavonoid content was 27.65 mg QE/g extract, while the total phenolic content was reported as 27.94 μ g GAE/g extract. Both calibration curves demonstrated high coefficients of determination, with R^2 values of 0.9903 and 0.9914, respectively.

3.3 Effect on Body Weight

The normal-control group demonstrated relatively stable body weight during the experimental period. The disease-control group showed progressive weight gain, increasing from 180 ± 1.50 g at day 0 to 225 ± 0.63 g at day 36.

After treatment, body weight declined in the standard and extract-treated groups. At day 36, the reported body weights were:

Group	Day 36 body weight (g)
Normal	185 ± 1.1
Disease	225 ± 0.63
Standard	179 ± 1.50
ECG 200 mg/kg	185 ± 0.52
ECG 400 mg/kg	183 ± 0.62

The 400 mg/kg dose therefore demonstrated a marked reduction in PCOS-associated weight gain.

3.4 Effect on Ovarian and Uterine Weight

The disease-control group showed an increase in ovarian weight and reduction in uterine weight compared with normal controls.

Group	Ovary weight	Uterus weight
Normal control	94.97 ± 8.91	147.54 ± 9.00
Disease control	157.59 ± 6.35	125.34 ± 7.39
Standard control	127.25 ± 4.32	144.76 ± 10.18
ECG 200 mg/kg	134.44 ± 3.67	140.24 ± 8.73
ECG 400 mg/kg	126.32 ± 5.64	141.35 ± 5.39

Treatment with ECG reduced ovarian weight and increased uterine weight toward normal values. The higher dose showed greater improvement.

3.5 Effect on Reproductive Hormones

Letrozole administration produced substantial hormonal disturbances. Testosterone and LH were increased, whereas progesterone, estradiol, and FSH were reduced.



Group	Testosterone	Progesterone	Estradiol	FSH	LH
Normal	1.25 ± 0.251	30.17 ± 2.61	34.75 ± 1.23	26.00 ± 3.42	7.28 ± 0.65
Disease	2.85 ± 0.523	13.22 ± 1.35	10.62 ± 1.80	12.45 ± 1.31	16.67 ± 0.87
Standard	1.05 ± 0.134	29.52 ± 1.85	30.95 ± 2.05	22.65 ± 2.04	8.30 ± 0.45
ECG 200 mg/kg	1.89 ± 0.178	22.80 ± 2.28	25.88 ± 1.12	16.00 ± 1.51	10.60 ± 0.75
ECG 400 mg/kg	1.16 ± 0.172	25.55 ± 3.32	28.78 ± 1.12	20.00 ± 2.09	9.20 ± 0.62

ECG treatment improved the hormonal disturbances in a dose-related manner, with the 400 mg/kg group showing greater normalization than the 200 mg/kg group.

3.6 Effect on Lipid Profile

The disease-control group showed reduced HDL and increased triglycerides and total cholesterol.

Group	HDL (mg/dL)	Triglycerides (mg/dL)	Total cholesterol*
Normal	60.07 ± 1.0	79.01 ± 1.8	200.6 ± 6.55
Disease	38.02 ± 1.2	122.02 ± 1.91	242 ± 7.88
Standard	55.3 ± 1.30	91.1 ± 1.1	215 ± 10.23
ECG 200 mg/kg	50.02 ± 1.30	102.2 ± 1.8	225.06 ± 5.65
ECG 400 mg/kg	52.3 ± 1.0	96.2 ± 1.0	220.02 ± 4.52

Treatment with ECG improved the lipid abnormalities induced by letrozole. The 400 mg/kg dose produced greater improvement than the 200 mg/kg dose.

3.7 Effect on Blood Glucose

Blood glucose increased progressively in the disease-control group. At day 36, glucose was 97 ± 2.2 in the disease group compared with 79.00 ± 2.2 in the normal group.

*The thesis labels this parameter as mg/mL; the manuscript retains the source value but this unit should be verified against the original laboratory record before journal submission.

Day	Normal	Disease	Standard	ECG 200 mg/kg	ECG 400 mg/kg
0	74.66 ± 3.0	78.00 ± 3.02	73.66 ± 1.25	73.66 ± 1.60	73 ± 3.02
7	77.50 ± 1.20	82 ± 1.20	80.00 ± 2.36	82 ± 1.22	81 ± 1.20
14	78.66 ± 1.38	86 ± 1.3	85 ± 2.24	87 ± 1.54	84 ± 1.38
21	78.00 ± 1.22	92 ± 1.22	90 ± 3.34	91 ± 0.42	90 ± 1.22
28	79.33 ± 1.60	95 ± 1.60	83.0 ± 2.21	88 ± 0.63	86 ± 1.60
36	79.00 ± 2.2	97 ± 2.2	81 ± 3.21	87 ± 0.54	85 ± 2.2

Both doses of ECG reduced the elevated glucose levels, with ECG 400 mg/kg showing greater improvement.

The disease group demonstrated marked reductions in GSH and CAT levels.

3.8 Effect on Antioxidant Parameters

Group	GSH	CAT
Normal	7.9 ± 0.3	20.3 ± 0.8
Disease	3.9 ± 0.50	13.4 ± 1.2
Standard	6.0 ± 0.9	19.6 ± 0.5
ECG 200 mg/kg	5.23 ± 0.25	17.2 ± 0.8



ECG 400 mg/kg	5.98 ± 0.28	18.8 ± 0.6
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Treatment with ECG increased GSH and CAT levels compared with the disease-control group, suggesting improvement in the antioxidant status of ovarian tissue.

4. DISCUSSION

The present investigation evaluated the effects of ethanolic leaf extract of *Coccinia grandis* in a letrozole-induced PCOS model. The experimental findings indicate that letrozole successfully produced several characteristic reproductive and metabolic alterations, including increased body weight, increased ovarian weight, decreased uterine weight, hormonal imbalance, hyperglycemia, dyslipidemia, reduced antioxidant defense, and cystic ovarian morphology.

The phytochemical evaluation demonstrated the presence of alkaloids, flavonoids, steroids, phenols, cardiac glycosides, and tannins. The extract also contained measurable levels of flavonoids and phenolic compounds. These phytochemical classes may contribute to antioxidant and metabolic effects; however, the present study did not isolate individual compounds or establish their direct molecular mechanisms.

The progressive increase in body weight observed in the disease-control group was consistent with the metabolic disturbances associated with the experimental PCOS model. Treatment with ECG reduced body weight gain, particularly at 400 mg/kg. The improvement may be associated with the metabolic effects of the plant extract, although the precise mechanism was not determined in the present investigation.

Changes in reproductive organ weights further supported the protective effect of the extract. Letrozole increased ovarian weight while reducing uterine weight. These changes may reflect cystic

follicular development and altered estrogenic activity. ECG treatment shifted both parameters toward normal values, with the 400 mg/kg dose demonstrating the most pronounced effect.

The hormonal findings were particularly relevant. Letrozole increased testosterone and LH while decreasing progesterone, estradiol, and FSH. These alterations are consistent with disruption of ovarian steroidogenesis and the hypothalamic-pituitary-ovarian axis. ECG treatment partially normalized these hormonal changes. The higher dose produced a greater reduction in testosterone and LH and greater recovery of progesterone, estradiol, and FSH than the lower dose.

The metabolic effects of the extract were also evident from the lipid and glucose findings. The disease-control group showed reduced HDL and increased triglyceride and total cholesterol levels. ECG improved these changes, with the 400 mg/kg dose producing better results than 200 mg/kg. Similarly, progressive hyperglycemia in the disease-control group was attenuated by ECG treatment.

Oxidative stress is an important component of PCOS-associated ovarian dysfunction. The disease-control group showed marked reduction in GSH and CAT, indicating impaired antioxidant defense. Both doses of ECG improved these antioxidant parameters, with 400 mg/kg producing greater restoration. The presence of flavonoid and phenolic constituents in the extract may contribute to antioxidant activity, although this proposed mechanism requires direct experimental confirmation.

Histopathological examination provided morphological support for the biochemical findings. The disease-control ovaries showed numerous cystic follicles, thin granulosa cell layers, and absence of corpus luteum. ECG



treatment improved follicular development and restored corpus luteum formation. The effect was particularly pronounced at 400 mg/kg, where the ovarian architecture approached that of the normal control group.

Overall, the results indicate a broad pharmacological effect of *Coccinia grandis* leaf extract involving reproductive, metabolic, and antioxidant parameters. The greater efficacy of the 400 mg/kg dose compared with 200 mg/kg suggests a dose-related response within the tested range.

CONCLUSION

The present study demonstrates that ethanolic leaf extract of *Coccinia grandis* exhibited promising protective and therapeutic effects in female rats with letrozole-induced PCOS. The extract improved body weight, reproductive organ weights, hormonal disturbances, lipid abnormalities, blood glucose levels, antioxidant status, and ovarian histopathological alterations.

Among the tested doses, 400 mg/kg showed the most pronounced overall activity and approached the effects observed with the standard drug metformin for several evaluated parameters.

The findings support further investigation of *Coccinia grandis* as a potential plant-derived complementary approach for PCOS. However, the current findings are limited to an experimental animal model. Further work should focus on isolation and characterization of the active phytoconstituents, molecular mechanism studies, detailed toxicity evaluation, pharmacokinetic investigations, and ultimately appropriately designed clinical studies.

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HOW TO CITE: Shubham Gupta, Dr. Varsha Bandil, Rajesh Asija, *Phytochemical and Pharmacological Evaluation of Coccinia grandis Leaf Extract on Letrozole-Induced Polycystic Ovary Syndrome in Female Rats*, *Int. J. of Pharm. Sci.*, 2026, Vol 4, Issue 10, 1680-1687. <https://doi.org/10.5281/zenodo.23332424>

