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Role of Camellia Sinensis in Polycystic Ovary Syndrome: A Systematic Review

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Abstract: Polycystic Ovary Syndrome (PCOS) is one of the most common endocrine-metabolic disorders affecting women of reproductive age and has significant impacts on hormonal, metabolic, and reproductive functions. Conventional therapies generally focus on managing symptoms but do not comprehensively target the underlying pathogenesis of PCOS. This systematic review aimed to evaluate the potential effects of *Camellia sinensis* and its bioactive compounds on PCOS based on in vivo experimental studies. The review was conducted according to PRISMA 2020 guidelines using databases including PubMed, ScienceDirect, and Google Scholar. Eligible studies involved validated animal models of PCOS induced by letrozole, estradiol valerate, or similar agents, with interventions consisting of green tea extract, catechins, or epigallocatechin-3-gallate (EGCG). Risk of bias was assessed using the SYRCLE Risk of Bias tool for animal studies. Six in vivo studies met the inclusion criteria. The findings indicate that *Camellia sinensis* may improve hormonal imbalance, ovarian histomorphology, folliculogenesis, insulin resistance, inflammatory markers, and oxidative stress in PCOS models. One study also demonstrated enhanced metabolic and histological outcomes when EGCG was combined with vitamin D. However, the evidence remains preclinical, heterogeneous, and limited in several outcome domains. Further well-designed human studies are necessary to confirm its therapeutic potential in PCOS management.

Keyword: Camellia Sinensis; Epigallocatechin Gallate; Insulin Resistance; Oxidative Stress; Polycystic Ovary Syndrome.

1. INTRODUCTION

Women in their reproductive years are disproportionately affected by PCOS, a complicated, polygenic endocrine-metabolic condition. Estimates of its worldwide occurrence vary from 8% to 13%, depending on the diagnostic criteria applied (Bulsara et al., 2021; Teede et al., 2023). According to the Rotterdam 2003 consensus criteria, which are still the most popular diagnostic criteria in contemporary clinical and research contexts. The illness is distinguished by three key characteristics: polycystic ovarian morphology on ultrasonography, clinical or biochemical hyperandrogenism, and ovulatory dysfunction (Teede et al., 2023). Insulin resistance, type 2 diabetes, dyslipidemia, non-alcoholic fatty liver disease, and increased cardiovascular risk are only a few of the major cardiometabolic consequences of PCOS, a chronic, systemic disorder that affects more than just reproduction. Additionally, it has significant psychological morbidity, such as depression, anxiety, and a poorer quality of life in connection to one's health (Bulsara et al., 2021; Rashid et al., 2022).

Peripheral insulin resistance, excessive androgen biosynthesis of primarily ovarian origin, chronic low-grade systemic inflammation, and dysregulation of the HPO axis all contribute to the pathophysiology of PCOS by sustaining a self-sustaining cycle of hormonal and metabolic disruption (Rashid et al., 2022; Siddiqui et al., 2024). Hyperinsulinaemia, arising as a compensatory response to impaired insulin sensitivity, further amplifies ovarian androgen

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production through upregulation of the cytochrome P450c17α enzyme complex and enhancement of luteinising hormone (LH) receptor responsiveness, generating a central pathogenic feedback loop that underpins the reproductive and metabolic phenotypes of the syndrome (Baptiste et al., 2010; Rosenfield & Ehrmann, 2016). Current pharmacological management strategies, including oral contraceptive pills, metformin, anti-androgens, and ovulation induction agents, address individual symptomatic domains but are constrained by narrow mechanistic breadth, suboptimal tolerability profiles, and the absence of disease-modifying effects, thereby necessitating investigation of complementary therapeutic modalities that simultaneously target multiple pathogenic pathways (Bulsara et al., 2021; Teede et al., 2023).

Within the domain of evidence-based botanical medicine, Camellia sinensis (green tea) has emerged as a pharmacologically compelling candidate for the adjunctive management of PCOS-related hormonal and metabolic disturbances (Hazimeh et al., 2023). Epigallocatechin-3-gallate (EGCG), epigallocatechin (EGC), epicatechin gallate (ECG), and epicatechin (EC) are the primary bioactive components of green tea, also referred to as catechins. The most prevalent and pharmacologically active of these is EGCG (Hazimeh et al., 2023; Siddiqui et al., 2024). EGCG has pleiotropic biological effects at the molecular level that are mechanistically relevant to the pathophysiology of PCOS. These effects include: lowering IRS-1 serine phosphorylation, which restores glucose transporter type-4 (GLUT-4) translocation and improves peripheral insulin sensitivity; suppressing nuclear factor kappa-B (NF-κB) signalling and the downstream pro-inflammatory cytokine cascade, which includes interleukin-6 (IL-6) and TNF-α (Hazimeh et al., 2023; Siddiqui et al., 2022). Furthermore, EGCG demonstrates anti-androgenic properties through inhibition of 5-alpha-reductase activity, competitive engagement of androgen receptors, and suppression of steroidogenic enzymes implicated in ovarian androgen overproduction, rendering it a mechanistically coherent candidate for attenuating hyperandrogenism in PCOS(Liu et al., 2024; Waltner-Law et al., 2002).

An important rationale for the present systematic review is the recognised paucity of rigorous randomised controlled trials (RCTs) in human populations examining the therapeutic role of C. sinensis in PCOS. The conduct of human RCTs in this context is constrained by ethical, logistical, and methodological considerations including challenges in achieving standardised disease induction, the inability to perform invasive outcome assessments, potential confounding from lifestyle variables, and limitations in direct ovarian tissue analysis .[9] In this context, in vivo experimental animal studies occupy a foundational and indispensable

role, providing the mechanistic evidence base necessary to characterise therapeutic pathways, evaluate dose-response relationships, assess tissue-level effects, and generate proof-of-concept data upon which human trials can be rationally designed (Liu et al., 2024; Yavangi et al., 2024). Animal PCOS models, particularly those induced by letrozole (a selective aromatase inhibitor) or estradiol valerate, accurately summarize the main hormonal, metabolic, and reproductive aspects of the human condition, such as increased androgen levels, disturbed folliculogenesis, insulin resistance, and persistent inflammation (Yavangi et al., 2024). Accordingly, a systematic and methodologically rigorous synthesis of in vivo evidence is both scientifically justified and urgently needed to consolidate the existing knowledge base and inform the design of future clinical investigations (Hazimeh et al., 2023; Teede et al., 2023).

2. METHODS

Study Design

According to the PRISMA 2020 standards, this study was organized and carried out as a systematic review (Page et al., 2021). The review was designed to comprehensively synthesise in vivo (animal) experimental evidence addressing the therapeutic role of Camellia sinensis and its bioactive derivatives in established animal models of polycystic ovary syndrome (PCOS). In vivo animal studies were specifically selected as the study design of interest because well-designed and adequately powered RCTs in human populations examining this intervention remain limited, and direct mechanistic assessment of ovarian tissue-level changes is not ethically feasible in human participants. Animal models of PCOS, particularly those induced through letrozole or estradiol valerate, reliably reproduce the cardinal hormonal, metabolic, and morphological features of the human syndrome, making them invaluable for mechanistic investigation and therapeutic proof-of-concept evaluation. Eligibility criteria, primary and secondary outcome measures, and the analytical approach were pre-specified prior to commencement of literature screening to ensure methodological transparency and minimise post-hoc decision-making

PICO Framework

To ensure systematic, transparent, and repeatable study selection that was particularly appropriate for in vivo experimental research, the PICO framework was utilized to operationalize eligibility criteria.

Table 1. PICO framework defining eligibility criteria and outcome measures for the systematic review.

Component	Operational Definition
Population (P)	Female animal models of PCOS (rats or mice) induced using validated methods (e.g., letrozole, estradiol valerate, DHEA, or testosterone propionate).
Intervention (I)	Administration of Camellia sinensis or its derivatives (green tea extract, catechins, EGCG) in any form, dose, or route, either as the primary intervention or as a distinct, analysable treatment arm.
Comparator (C)	PCOS animal models receiving no treatment, placebo/vehicle, or standard pharmacological therapy (e.g., metformin, clomiphene citrate).
Outcomes (O)	Primary: serum testosterone levels. Secondary: reproductive hormones, inflammatory markers, metabolic parameters, oxidative stress markers, and ovarian morphology.

PCOS = polycystic ovary syndrome; EGCG = epigallocatechin-3-gallate.

Literature Search Strategy

Due to their extensive coverage of pharmacology, reproductive biology, and phytotherapy, PubMed (MEDLINE), ScienceDirect, and Google Scholar were chosen for a thorough electronic literature search. Boolean operators were used in the search technique to mix free-text keywords with regulated vocabulary (MeSH terms). For in vivo research, the following search term was employed: ("Camellia sinensis" OR "green tea" OR "green tea extract" OR "epigallocatechin gallate" OR "EGCG" OR "catechin") AND ("polycystic ovary syndrome" OR "PCOS") AND ("rat" OR "mice" OR "animal model" OR "in vivo").

Articles in English and Indonesian were included. No strict publication year limit was applied initially; however, studies older than 15 years were critically appraised for methodological quality. To lessen publication bias, the included articles' reference lists and pertinent evaluations were thoroughly reviewed. The Cochrane Handbook for Systematic Reviews of Interventions was followed in the search procedure. Two reviewers separately completed the screening and eligibility evaluation; differences were settled by discussion or a third reviewer.

Inclusion and Exclusion Criteria

Inclusion Criteria

Studies that satisfied the following requirements were included:

a. Original experimental in vivo (animal) studies.
b. Studies employing validated animal models of PCOS (female rats or mice induced by letrozole, estradiol valerate, testosterone propionate, DHEA, or other established induction

methods).

c. Studies administering Camellia sinensis or its bioactive derivatives (green tea extract, catechins, EGCG) either as the primary intervention or as a distinct, analysable treatment arm.
d. Studies reporting at least one outcome aligned with the predefined PICO framework (testosterone, gonadotropins, inflammatory markers, metabolic parameters, or ovarian histopathology).
e. Original research articles with full-text availability.
f. Articles published in English or Indonesian.

Exclusion Criteria

Research that satisfied any of the following criteria was eliminated:

a. Non–in vivo studies: in vitro cell-line studies, human clinical studies (RCTs, cohort, cross-sectional, case reports), and computational studies.
b. Non-original articles include editorials, conference abstracts, narrative reviews, meta-analyses, and systematic reviews.
c. Studies not using a validated PCOS animal model.
d. Studies in which the effects of Camellia sinensis or its derivatives could not be isolated or meaningfully interpreted, such as multi-herbal formulations or combination therapies without a distinct, analysable Camellia sinensis treatment arm.
e. Studies reporting no outcome relevant to the study objectives.
f. Duplicate publications from the same study population (the most complete and recent report was retained).

Study Selection and Data Extraction

There were two phases to the study selection process. Initially, abstracts and titles were compared to the predetermined eligibility requirements. Second, full-text publications that were deemed possibly pertinent were evaluated for eventual inclusion. Two reviewers independently carried out the screening process, and conflicts were settled by discussion; if no agreement could be achieved, a third reviewer was consulted.

Using a standardized extraction form created specifically for this review, two reviewers independently extracted the data. Author, publication year, nation, species of animal, and sample size, PCOS induction method, treatment type, formulation of Camellia sinensis or its derivatives, dose, route of administration, duration of PCOS induction, duration of treatment, comparator group, and reported hormonal, metabolic, inflammatory, oxidative stress, and histomorphological outcomes were among the extracted items. Discussion and cross-

referencing with the source full-text articles were used to address any disparities in the derived data.

To improve comparability across studies, the review distinguished the duration of PCOS induction from the duration of treatment administration, as these were reported separately in several included animal studies.

Quality Assessment and Risk of Bias

Using the SYRCLE Risk of Bias Tool, a well-liked tool for animal studies, two reviewers independently evaluated the methodological quality and bias risk of included in vivo research (Hooijmans et al., 2014). Sequence generation, baseline characteristics, allocation concealment, random housing, blinding, outcome evaluation, inadequate data, selective reporting, and other potential biases are among the eleven criteria that the tool assesses. Every domain was categorized as having a bias risk of unknown, high, or low. A third reviewer was consulted or discussed in order to settle disagreements. A quantitative meta-analysis was not carried out since animal models, induction techniques, therapies, and outcome measures varied. Rather, the results were summarized using a systematic narrative synthesis.

3. RESULTS

The study selection process adhered to the PRISMA 2020 flow diagram. The initial electronic database search spanning PubMed, ScienceDirect, and Google Scholar turned up 1885 documents. 1748 distinct records were subjected to title and abstract screening against predetermined eligibility criteria after 137 duplicate entries were eliminated. A further 1711 records were excluded at this stage due to: non-animal study design (human RCTs, in vitro, reviews), absence of a validated PCOS model, use of non-Camellia sinensis interventions, or irrelevant topic and outcome reporting. After that, 37 full-text papers were obtained for a thorough eligibility evaluation; 31 of these were eliminated for the reasons listed below: in vitro design (n=4), human clinical studies (n=5), multi-herbal formulations with no isolable C. sinensis effect (n=9), non-PCOS model (n=11), and insufficient outcome data (n=2). The final qualitative synthesis contained six in vivo animal studies that met all eligibility requirements.

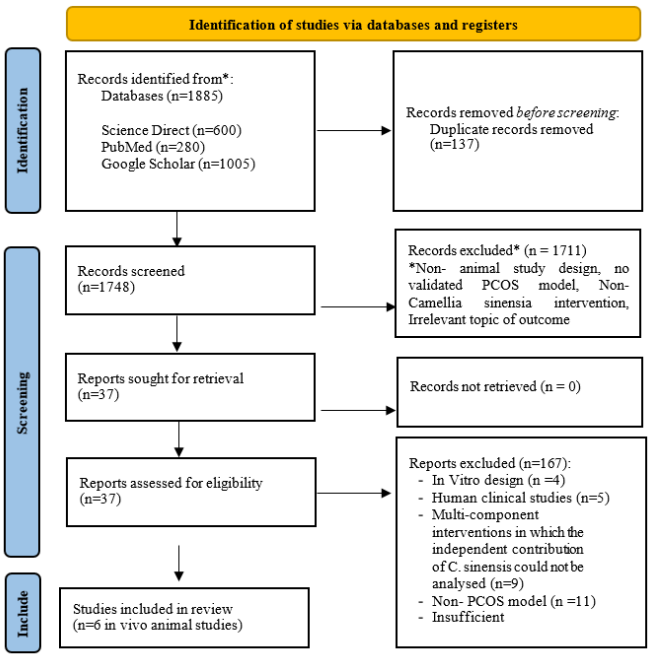

Figure 1. PRISMA 2020 flow diagram of study selection process.

Table 2. Characteristics of the included in vivo studies, including PCOS induction protocol and treatment duration.

Authors & Year	Country	Animal Model	Sample Size (n)	PCOS Induction Method + Duration	Treatment Duration	Intervention Form	Dose	Control Group	Outcomes Assessed	Key Finding
Ghafurniyan et al., 2015	Iran	Adult female Wistar rats (200 ± 20 g)	96	Daily subcutaneous estradiol valerate (2 mg/kg); PCOS confirmed after approximately 60 days	10 days	Hydro-alcoholic green tea extract	50, 100, and 200 mg/kg BW, intraperitoneally	Saline-treated sham control	FSH, LH, testosterone, insulin, glucose, HOMA-IR, BW, ovarian weight, histomorphometry	Significant decreases in LH, testosterone, glucose, and HOMA-IR; increased follicle counts; reduced cystic follicles; dose-dependent effects
Ghafurniyan et al., 2014	Iran	Adult female Wistar rats (200	96	Subcutaneous estradiol valerate (2 mg/kg); PCOS confirme	14 days	Hydro-alcoholic green tea extract	50, 100, and 200 mg/kg BW, intraperitoneally	Saline-treated sham control	IL-6, CRP (serum and ovarian tissue), histomorphometry	Significant reductions in IL-6 and CRP; improvement in follicular

		± 20 g)		d after approximately 60 days						layer thickness; 100 mg/kg was the most effective dose
Sadoughi & Rahbarian, 2017	Iran	Adult female Wistar rats (190 ± 8 g)	42	Single intramuscular estradiol valerate injection (4 mg/kg); induction duration not clearly reported	24 days	Aqueous green tea extract; catechin	Aqueous green tea extract 50 and 100 mg/kg IP; catechin 50 and 100 mg/kg IP	Clomiphene citrate 1.5 mg/kg	LH, FSH, estradiol, progesterone, testosterone, follicle counts (all stages), cystic follicles	Catechin 100 mg/kg reduced LH, estradiol, and testosterone; increased FSH and progesterone; improved follicle counts; effects were comparable to clomiphene
Puspita et al., 2019	Indonesia	Female Wistar rats (100–110 g; 3 months)	35	Testosterone propionate 1 mg/100 g BW IM for 28 days	14 days	Green tea extract	200, 400, and 800 mg/kg BW orally	Negative control (distilled water); positive Control (PCOS + distilled water)	Serum insulin levels; folliculogenesis (primary, secondary, tertiary, and de Graaf follicles)	Green tea extract 800 mg/kg significantly reduced insulin levels; follicle counts improved; dose-dependent effect
Khudhair et al., 2025	Iraq	Female rats (185–195 g)	24	Letrozole 1 mg/kg orally for 4 weeks	4 weeks (administered concurrently with letrozole)	Aqueous green tea extract	250 mg/kg orally	Distilled water (negative control); letrozole only (PCOS positive control); chasteberry 750 mg/kg	FSH, LH, prolactin (PRL), ovarian histopathology (H&E staining)	Significant increase in FSH; reductions in LH and PRL; decreased ovarian cyst size and number; restored follicular architecture and corpus luteum

Khudhair et al., 2025	Iraq	Female rats (185–195 g)	24	Letrozole 1 mg/kg orally for 4 weeks	4 weeks (administered concurrently with letrozole)	Aqueous green tea extract	250 mg/kg orally	Distilled water (negative control); letrozole only (PCOS positive control); chasteberry 750 mg/kg	FSH, LH, prolactin (PRL), ovarian histopathology (H&E staining)	Significant increase in FSH; reductions in LH and PRL; decreased ovarian cyst size and number; restored follicular architecture and corpus luteum
Siddiqui et al., 2025	India	Female Wistar rats (170–200 g; 6 weeks)	42	Letrozole 1 mg/kg/day orally (CMC) for 21 days	15 days	EGCG, vitamin D, CGA	EGCG 100 mg/kg/day ± vitamin D 25 mcg/kg/day orally for 15 days; CGA 120 mg/kg/day ± vitamin D	Healthy control (CMC); PCOS group (letrozole); metformin 300 mg/kg/day (positive control)	Testosterone, estradiol, progesterone, FSH, LH, glucose, insulin, HOMA-IR, AGEs, lipid profile, LFT, vitamin D, protein oxidation, LPO, OSI, ROS, RNS, antioxidant enzymes, DNA damage, ovarian histology	EGCG + vitamin D showed the broadest improvements, including reduced testosterone, glucose, and HOMA-IR; decreased ROS/RNS and DNA damage; restored ovarian morphology; effects were comparable to metformin

GTE = green tea extract; EGCG = epigallocatechin-3-gallate; CGA = chlorogenic acid; VitD = vitamin D; IP = intraperitoneal; SC = subcutaneous; IM = intramuscular; BW = body weight; LPO = lipid peroxidation; OSI = oxidative stress index; ROS = reactive oxygen species; RNS = reactive nitrogen species; AGEs = advanced glycation end-products; HOMA-IR = homeostatic model assessment of insulin resistance; CMC = carboxymethylcellulose; LFT = liver function test; H&E = haematoxylin and eosin.

Table 3. Summary of main findings from included in vivo animal studies.

Author (Year)	Results
(Ghafurniyan et al., 2015)	In estradiol valerate–induced PCOS rats, intraperitoneal administration of hydro-alcoholic green tea extract (50–200 mg/kg) for 10 days significantly reduced LH, testosterone, insulin, fasting glucose, and HOMA-IR in a dose-dependent manner. Histomorphometric analysis showed increased normal follicle development and corpus luteum formation, along with a marked reduction in cystic follicles, which normalized at 200 mg/kg. Treatment also significantly decreased body and ovarian weights, with no reported adverse effects.
[1](Ghafurniyan et al., 2014)	Estradiol valerate–induced PCOS significantly increased serum CRP and IL-6 levels compared to healthy controls, indicating a low-grade inflammatory state. Intraperitoneal administration of hydro-alcoholic green tea extract (50–200 mg/kg) for 14 days significantly reduced CRP at all doses, with the greatest reduction in IL-6 observed at 100 mg/kg (from ~50 to ~30 pg/mL). Histopathological analysis showed improved granulosa and theca cell architecture, reduced cystic follicles and stromal proliferation, and reappearance of corpus luteum, with no observed adverse effects.
(Sadoughi and Rahbarian, 2017)	In estradiol valerate–induced PCOS rats, intraperitoneal administration of aqueous GTE (100 mg/kg) and catechin (50–100 mg/kg) for 24 days significantly reduced LH, estradiol, and testosterone levels, while increasing FSH and progesterone. Catechin at 100 mg/kg produced hormonal effects comparable to clomiphene citrate (1.5 mg/kg). Folliculogenesis improved, as indicated by increased pre-antral to pre-ovulatory follicles and decreased cystic follicles in a dose-dependent manner. However, GTE at 50 mg/kg showed no significant effect. Catechin exhibited a favorable safety profile with no observed toxicity.
(Puspita et al., 2020)	In testosterone propionate–induced insulin-resistant PCOS rats, oral administration of aqueous green tea extract (200–800 mg/kg) for 14 days reduced serum insulin in a dose-dependent manner, with a significant effect observed only at 800 mg/kg ($p<0.05$). While all doses increased follicle counts across developmental stages, a statistically significant enhancement in folliculogenesis occurred only at the highest dose. A clear dose–response relationship was observed, with no reported adverse effects.
(Khudhair et al., 2025)	In letrozole-induced PCOS rats, oral administration of green tea extract (250 mg/kg) for four weeks significantly increased FSH and reduced LH and prolactin levels compared to PCOS controls. Histological analysis showed reduced cystic follicles and restoration of normal ovarian architecture, including corpus luteum and Graafian follicles. The effects were comparable to chasteberry extract (750 mg/kg), with no significant differences between treatments and no observed adverse effects.
(Siddiqui et al., 2025)	In letrozole-induced PCOS rats, combined oral administration of vitamin D (25 mcg/kg/day) and EGCG (100 mg/kg/day) for 15 days produced the most comprehensive therapeutic effects, comparable to or exceeding those of metformin (300 mg/kg/day). Testosterone decreased by 53.4%, while estradiol and progesterone were significantly restored. Fasting glucose, AGE levels, and HOMA-IR were markedly reduced, alongside significant declines in triglycerides and total cholesterol. Oxidative stress and ROS were substantially suppressed, with marked reductions in DNA fragmentation and significant restoration of antioxidant enzyme activities.

EGCG = epigallocatechin-3-gallate; GTE = green tea extract; HOMA-IR = homeostatic model assessment of insulin resistance; AGE = advanced glycation end-products; ROS = reactive oxygen species; OSI = oxidative stress index; SOD = superoxide dismutase; GPx = glutathione peroxidase; PON-1 = paraoxonase-1; CRP = C-reactive protein; IL-6 = interleukin-6; LH = luteinising hormone; FSH = follicle-stimulating hormone; IP = intraperitoneal.

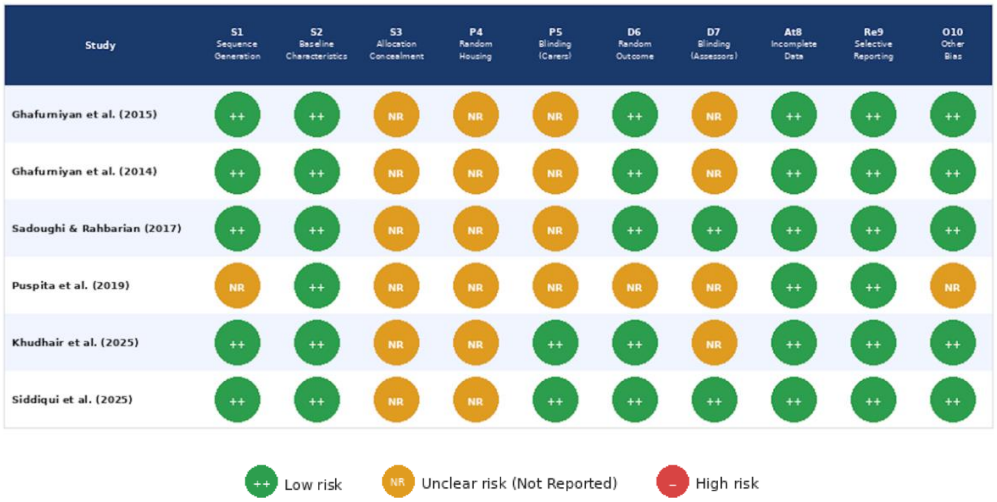

Figure 2. Risk of bias assessment of animal studies SYRCLE Risk of Bias Tool Green = low risk; Yellow = unclear risk; Red = high risk.

Effects on Hormonal Profiles and Gonadotropins

Across the included in vivo studies, Camellia sinensis preparations consistently demonstrated significant hormonal modulatory effects in PCOS animal models. Ghafurniyan found that after ten days of intraperitoneal administration, hydro-alcoholic green tea extract produced dose-dependent, statistically significant decreases in serum LH and testosterone concentrations in estradiol valerate-induced PCOS rats, with no discernible change in FSH at the doses assessed (Ghafurniyan et al., 2015). Sadoughi demonstrated that both aqueous green tea extract (100 mg/kg) and isolated catechin (50 and 100 mg/kg) significantly reduced serum LH, estradiol, and testosterone while concurrently elevating FSH and progesterone concentrations in the estradiol valerate PCOS model (Sadoughi and Rahbarian, 2017). Notably, catechin at 100 mg/kg produced hormonal restoration statistically comparable to clomiphene citrate, the positive pharmacological comparator employed in this study. Khudhair confirmed these findings in the letrozole-induced PCOS model, with green tea extract (250 mg/kg) significantly increasing FSH while reducing LH and prolactin (Khudhair et al., 2025). Siddiqui observed that EGCG combined with vitamin D most effectively restored the hormonal profile decreasing testosterone by 53.4% and restoring estradiol and progesterone levels toward control values exhibiting a magnitude of effect comparable to metformin in the letrozole model (Siddiqui et al., 2025).

Effects on Metabolic Parameters and Insulin Resistance

Several studies reported substantial improvements in metabolic indices following C. sinensis administration. Ghafurniyan showed statistically significant and dose-dependent decreases in the HOMA-IR insulin resistance index, serum insulin concentration, and fasting

blood glucose in all three green tea extract dose groups (50, 100, and 200 mg/kg) (Ghafurniyan et al., 2015). Puspita found that in the testosterone propionate-induced insulin-resistant PCOS model, green tea extract at 800 mg/kg significantly decreased blood insulin levels ($p<0.05$), with lower doses producing non-significant reductions (Puspita et al., 2020). Siddiqui provided the most comprehensive metabolic assessment, demonstrating that EGCG combined with vitamin D significantly reduced fasting blood glucose (from 185.8±4.99 to 128.8±5.58 mg/dL), attenuated advanced glycation end-product (AGE) formation by 55.35%, normalised serum insulin concentration, and restored the HOMA-IR index to near-control values effects statistically comparable to metformin. Additionally, total cholesterol was reduced by 55.3% and triglycerides by 75.6% in the EGCG+vitamin D group relative to untreated PCOS animals (Siddiqui et al., 2022).

Effects on Ovarian Morphology and Folliculogenesis

Histopathological and morphometric ovarian assessments demonstrated consistent beneficial effects of C. sinensis across included studies. Ghafurniyan discovered that administering green tea extract significantly decreased the number of cystic follicles while simultaneously and dose-dependently raising the numbers of corpus luteum, primary, pre-antral, antral, and pre-ovulatory follicles (Ghafurniyan et al., 2015). At the maximum dose (200 mg/kg), the cystic follicle burden fully recovered to normal. Puspita confirmed that in insulin-resistant PCOS mice, 800 mg/kg of green tea extract significantly increased folliculogenesis at all stages of follicle development (primary, secondary, tertiary, and de Graaf follicles) (all $p<0.05$) (Puspita et al., 2020). Khudhair demonstrated that using green tea extract significantly reduced the number and size of ovarian cysts, restored normal ovarian parenchymal architecture(Khudhair et al., 2025). These results were in close agreement with those of the comparator group treated with chasteberries. Siddiqui documented comparable histological restoration in the EGCG+vitamin D group, with ovarian sections demonstrating re-emergence of primary follicles, mature Graafian follicles, and corpus luteum alongside significant reduction in follicular cysts matching the recovery profile observed with metformin (Siddiqui et al., 2025).

Effects on Inflammatory Markers

Ghafurniyan carried out a thorough analysis of green tea's anti-inflammatory properties in the PCOS model, demonstrating that PCOS induction via estradiol valerate produced significantly elevated serum IL-6 and CRP concentrations relative to healthy controls (Ghafurniyan et al., 2015). Treatment with green tea extract at 100 mg/kg produced the most significant reduction in IL-6 (from approximately 50 pg/mL in PCOS controls to approximately

30 pg/mL), while all three doses (50, 100, 200 mg/kg) significantly attenuated CRP levels. The study further identified improvements in follicular layer architecture consistent with the anti-inflammatory mechanism. (Siddiqui et al., 2025) offered supporting data showing that EGCG + vitamin D dramatically reduced levels of reactive nitrogen species (RNS, nitric oxide) and reactive oxygen species (ROS, as determined by DCFH-DA fluorescence). ROS reduction reached 87.8% in comparison to untreated PCOS animals, which was comparable to the 89.3% reduction seen with metformin.

Effects on Oxidative Stress and Antioxidant Defence

Restoration of FSH and progesterone across multiple studies, aligns with the known oestrogenic and anti-androgenic properties of catechins. The mechanism underpinning androgen reduction involves the capacity of EGCG to competitively inhibit aromatase enzyme activity a finding corroborated by independent in vitro evidence demonstrating dose-dependent aromatase inhibition by green tea catechins as well as suppression of steroidogenic enzyme activity within ovarian theca cells (Satoh et al., 2002). The resultant reduction in ovarian androgen biosynthesis disrupts the principal feedback mechanism driving LH hypersecretion, restoring gonadotropin pulsatility toward the physiological pattern necessary for folliculogenesis to resume. The observation by Sadoughi (Sadoughi and Rahbarian, 2017) that catechin at 100 mg/kg produced hormonal restoration statistically comparable to clomiphene citrate is particularly noteworthy, suggesting that the isolated active catechin fraction possesses ovulation-inductive potency approaching that of a clinically established pharmacological agent. The restoration of progesterone levels is further indicative of restored corpus luteum function, representing a surrogate marker of successful ovulation a core therapeutic goal in PCOS.

The anti-inflammatory and antioxidant mechanistic axes represent the most extensively characterised pathways through which C. sinensis modulates PCOS pathophysiology. With high IL-6 and CRP acting as recognized indicators of this process and mechanistically linked to the persistence of insulin resistance and androgen excess, PCOS is becoming more well acknowledged as a condition of persistent low-grade

systemic inflammation (Rudnicka et al., 2020). EGCG inhibits NF-κB activation the master transcriptional regulator of pro-inflammatory cytokine expression through dual mechanisms: direct suppression of IKKβ kinase activity and inhibition of p38 MAPK and JNK signalling pathways that sustain cytokine transcription. The data from Ghafurniyan et al. (2014) (Ghafurniyan et al., 2014) this mechanism is clearly validated by showing that green tea extract administration significantly lowers blood IL-6 and CRP in PCOS rats. Concurrently, the

capacity of EGCG to directly scavenge reactive oxygen species through its polyphenolic hydroxyl groups, to activate the Nrf2-Keap1 cytoprotective pathway, and to upregulate endogenous antioxidant enzyme activity (SOD, catalase, GPx, GR, PON-1) comprehensively addresses the oxidative burden that characterises PCOS-affected ovarian tissue (Siddiqui et al., 2025). The profound reduction in DNA fragmentation documented by Siddiqui et al (Siddiqui et al., 2025) exceeding that achieved by metformin is of particular clinical relevance given the association between oxidative DNA damage and impaired oocyte quality in PCOS.

The metabolic benefits of C. sinensis treatment, which include decreases in serum insulin, fasting blood glucose, HOMA-IR, and lipid parameters, are indicative of multi-pathway insulin-sensitizing processes that are important to the pathophysiology of PCOS. It has been shown that EGCG suppresses the activity of glucose-6-phosphatase (G-6-Pase), which prevents the liver from producing glucose, to phosphorylate insulin receptor tyrosine residues thereby generating insulin-mimetic signalling, and to upregulate GLUT-4 translocation through peroxisome proliferator-activated receptor (PPAR) binding (Siddiqui et al., 2025; Singh et al., 2010). Simultaneously, the catechins in green tea stimulate adiponectin secretion from adipocytes through PPAR activation, improving whole-body insulin sensitivity and reducing visceral fat accumulation (Ghafurniyan et al., 2015). Vitamin D, employed as a complementary agent in the Siddiqui et al. (2025) (Siddiqui et al., 2025)study, enhances insulin receptor expression and promotes intracellular calcium influx a process necessary for insulin-mediated GLUT-4 translocation providing a synergistic mechanism that may explain the superior metabolic outcomes observed in the EGCG+vitamin D combination group relative to EGCG administered alone. These insulin-sensitising effects are mechanistically important because hyperinsulinaemia directly amplifies androgen production in ovarian theca cells, meaning that metabolic normalisation exerts secondary beneficial effects on the hormonal phenotype of PCOS.

Although the included studies generally reported favourable effects of *Camellia sinensis* and its derivatives in PCOS animal models, it is important to interpret the evidence's strength cautiously. Not all studies assessed the same outcome domains, and

several findings were supported by only one or a small number of experiments. Inflammatory outcomes were evaluated in a limited subset of studies, and detailed oxidative stress parameters were reported most comprehensively in only one study. In addition, heterogeneity in animal species, induction methods, treatment regimens, formulations, doses, and outcome measures limits direct comparability across studies. Therefore, the present

findings support biological plausibility and potential therapeutic relevance, but they do not yet

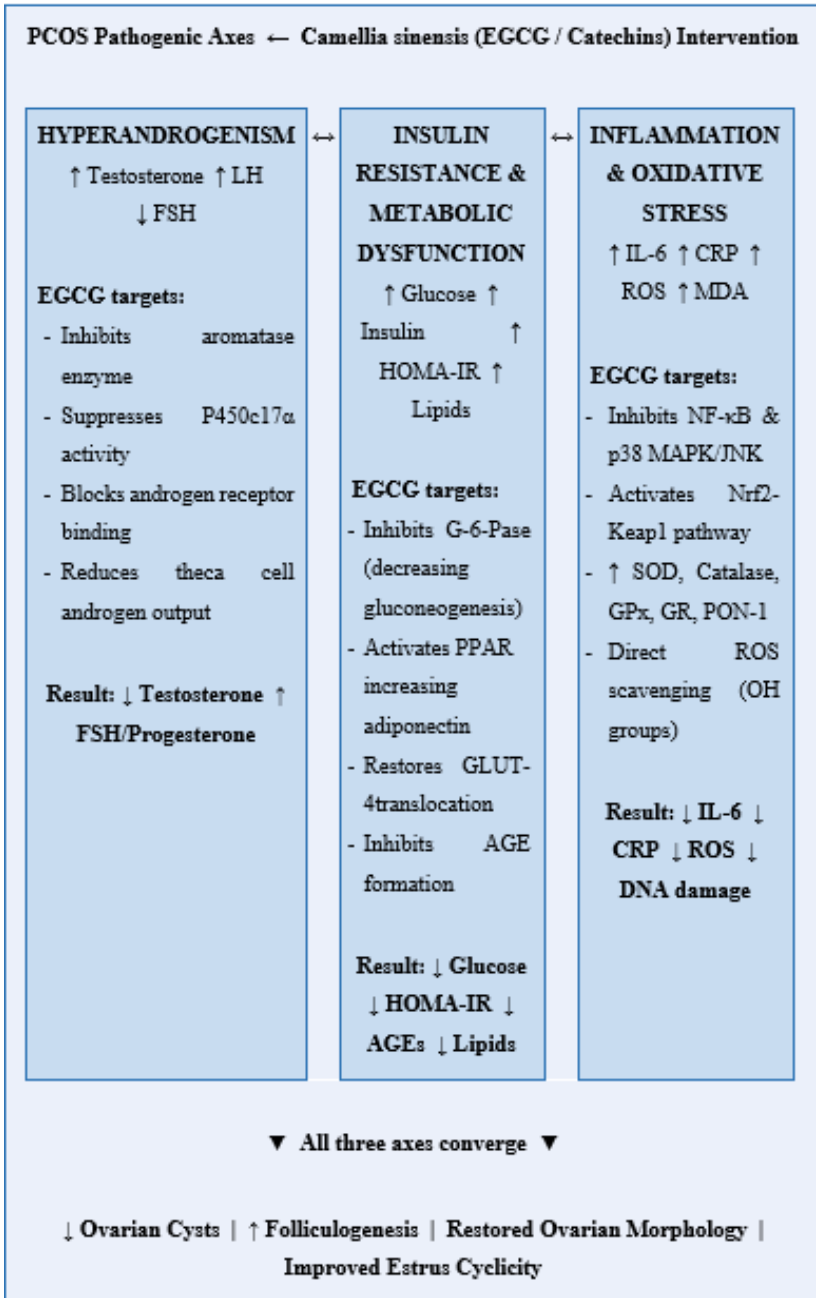

Figure 3. Mechanistic diagram illustrating the three principal pathogenic axes of PCOS and their modulation by Camellia sinensis (EGCG). Bidirectional arrows (↔) denote the interrelated and mutually reinforcing nature of the three pathogenic axes. EGCG = epigallocatechin-3-gallate; G-6-Pase = glucose-6-phosphatase; PPAR = peroxisome proliferator-activated receptor; GLUT-4 = glucose transporter type-4; AGE = advanced glycation end-products; NF-κB = nuclear factor kappa-B; Nrf2-Keap1 = nuclear factor erythroid 2-related factor 2; SOD = superoxide dismutase; GPx = glutathione peroxidase; GR = glutathione reductase; PON-1 = paraoxonase-1; ROS = reactive oxygen species; MDA = malondialdehyde; CRP = C-reactive protein; IL-6 = interleukin-6.

4. CONCLUSION

According to this comprehensive analysis of six in vivo investigations, Camellia sinensis and its key bioactive constituents, particularly catechins and EGCG, may improve several reproductive, metabolic, inflammatory, oxidative, and histomorphological features of PCOS in animal models. The most consistent findings were observed in ovarian morphology, folliculogenesis, and selected hormonal and metabolic parameters, whereas evidence for some domains, such as inflammation and oxidative stress, was more limited and less uniformly reported. Accordingly, the current evidence should be interpreted as supportive but still preliminary. Because all included studies were preclinical and varied substantially in design, dose, formulation, and outcome assessment, before definitive treatment findings can be made, more standardized animal research and carefully planned human clinical trials are required.

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