CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES
SJIF Impact Factor: 7.187
https://doi.org/10.5281/zenodo.18907141

Available online at: http://www.iajps.com Research Article

CLINICAL EVALUATION OF A MULTI-COMPONENT NUTRACEUTICAL FORMULATION IN WOMEN WITH POLYCYSTIC OVARY SYNDROME: A PROSPECTIVE OPEN-LABEL STUDY

***Venkata Suresh.P[a], Shagufta Khan[b], Rama rao.N[a], Grace Mishra[c]**

[a]Department of pharmaceutical analysis, Chalapathi Institute of Pharmaceutical Sciences, Lam, Guntur, Andhrapradesh, India.

[b]Department of pharmaceutical chemistry, Parul University, Vadodara, Gujarat, India.

[c]Miror Therapeutics Private Limited, Bengaluru, India.

Abstract:

Background: Polycystic ovary syndrome (PCOS) is a complex endocrine–metabolic disorder characterized by hyperandrogenism, insulin resistance, ovarian dysfunction, and stress-axis dysregulation. Nutraceutical interventions targeting multiple metabolic and hormonal pathways have gained attention as complementary therapeutic strategies.

Objective: To evaluate the short-term safety and clinical effects of a multi-component nutraceutical formulation in women diagnosed with PCOS.

Methods: Forty women aged 18–35 years fulfilling Rotterdam 2003 criteria were enrolled. Participants received one tablet daily for 30 days. Primary outcomes included fasting blood glucose (FBG), antral follicle count (AFC), ovarian volume, and serum cortisol. Secondary outcomes included WHOQOL-BREF scores and global clinical assessment. Paired statistical analysis compared baseline and Day 30 values.

Results: Thirty-eight participants completed the study. Significant reductions were observed in FBG (104.53 ± 9.56 to 98.06 ± 5.05 mg/dL), ovarian volume, AFC, and serum cortisol ($p < 0.05$). Quality-of-life scores improved across all domains. No serious adverse events were reported.

Conclusion: Short-term supplementation was associated with improvements in metabolic parameters, ovarian morphology, stress biomarkers, and quality-of-life indicators. Controlled randomized trials are required to confirm these preliminary findings.

Keywords: Polycystic ovary syndrome, nutraceutical, ovarian morphology, cortisol, insulin resistance, quality of life.

Corresponding author:

Venkata Suresh.P,

Department of pharmaceutical analysis,
Chalapathi Institute of Pharmaceutical Sciences,
Lam, Guntur, Andhrapradesh, India.
sureshpharma78@gmail.com

QR CODE

Please cite this article in press Venkata Suresh.Pet al., Clinical Evaluation Of A Multi-Component Nutraceutical Formulation In Women With Polycystic Ovary Syndrome: A Prospective Open-Label Study., Indo Am. J. P. Sci, 2026; 13(03).

INTRODUCTION:

Polycystic ovary syndrome (PCOS) is one of the most common endocrine–metabolic disorders affecting women of reproductive age and represents a major contributor to infertility and long-term metabolic morbidity worldwide. Prevalence estimates range between 8–13% globally [1], depending on diagnostic criteria and ethnicity. Although originally described as a reproductive condition characterized by hyperandrogenism and menstrual irregularity, PCOS is now recognized as a systemic disorder involving metabolic dysfunction, chronic low-grade inflammation, oxidative stress, and neuroendocrine imbalance.

The Rotterdam criteria define PCOS by the presence of at least two of the following: oligo- or anovulation, clinical or biochemical hyperandrogenism, and polycystic ovarian morphology on ultrasonography. However, diagnostic criteria do not fully capture the metabolic complexity of the condition [2-3].

A substantial proportion of women with PCOS demonstrate insulin resistance independent of body mass index, suggesting intrinsic defects in insulin signaling pathways. Hyperinsulinemia enhances ovarian theca cell androgen synthesis via activation of the PI3K/Akt and MAPK pathways, while simultaneously suppressing hepatic sex hormone-binding globulin production, thereby increasing circulating free testosterone levels. This endocrine–metabolic interaction contributes to follicular arrest, increased antral follicle count, and enlarged ovarian volume. Beyond insulin resistance, oxidative stress has emerged as a critical pathogenic mechanism. Elevated levels of reactive oxygen species and reduced antioxidant capacity have been documented in women with PCOS [4-7]. Oxidative stress may impair insulin receptor phosphorylation and steroidogenic enzyme regulation, further aggravating metabolic and reproductive dysfunction. These findings provide mechanistic justification for antioxidant-based interventions in PCOS.

Chronic low-grade inflammation is another key contributor. Elevated circulating inflammatory markers such as CRP and TNF-α have been reported in PCOS populations, independent of obesity. Inflammatory signaling may interfere with insulin receptor substrate activity, linking metabolic and inflammatory pathways. Therefore, interventions capable of modulating oxidative and inflammatory cascades may provide broader therapeutic benefit [8-10].

More recently, neuroendocrine dysregulation involving the hypothalamic–pituitary–adrenal (HPA) axis has been implicated. Altered cortisol secretion patterns and heightened stress responsivity have been observed in women with PCOS. Excess cortisol contributes to visceral adiposity and insulin resistance, creating a bidirectional amplification loop between stress physiology and metabolic dysfunction. Despite this, most clinical nutraceutical trials do not include cortisol or stress biomarkers as outcome measures, leaving an important mechanistic gap. Standard management strategies prioritize lifestyle modification, including calorie restriction and exercise. Pharmacological approaches such as metformin target insulin resistance and improve glycemic control. However, gastrointestinal intolerance, suboptimal adherence, and heterogeneous response profiles limit effectiveness in real-world settings [11-15]. Hormonal contraceptives address menstrual irregularity but do not correct underlying metabolic dysfunction. These limitations have stimulated interest in nutraceutical approaches that may complement lifestyle strategies.

Among nutraceutical agents, inositol isomers have received substantial attention. Myo-inositol and D-chiro-inositol function as secondary messengers in insulin signaling. A systematic review demonstrated improvements in ovulation rate and metabolic indices following inositol supplementation [16]. However, treatment durations typically ranged from 8 to 24 weeks, and ultrasonographic outcomes were not consistently reported. Curcumin, a polyphenolic compound with antioxidant and anti-inflammatory properties, has demonstrated improvements in glycemic control and inflammatory markers in randomized trials involving women with PCOS [17]. Similarly, omega-3 fatty acids have been shown to modestly improve insulin sensitivity and lipid profiles. Vitamin D supplementation has been associated with improvements in menstrual regularity in deficient women. While these interventions demonstrate potential, most studies focus on isolated compounds targeting single mechanistic pathways.

Given that PCOS pathophysiology involves simultaneous disturbances in insulin signaling, oxidative stress, inflammation, and stress-axis regulation, multi-component formulations may provide broader therapeutic coverage. However, evidence evaluating integrated nutraceutical combinations remains limited. Furthermore, few studies simultaneously assess metabolic, morphological, neuroendocrine, and quality-of-life outcomes within a short timeframe. Ovarian morphology represents a clinically relevant endpoint reflecting follicular dynamics. Yet, many nutraceutical studies emphasize biochemical markers without evaluating antral follicle count or ovarian volume. Inclusion of ultrasonographic

parameters enhances translational applicability by directly assessing ovarian structural response [18].

Quality-of-life impairment is increasingly recognized as a major component of PCOS burden. Women frequently report psychological distress, anxiety, and reduced social functioning. Comprehensive assessment using validated tools such as WHOQOL-BREF provides insight into patient-centered outcomes beyond biochemical change. Importantly, short-duration studies evaluating integrated endpoints are scarce. Most nutraceutical trials extend over 8–12 weeks or longer. Demonstration of early metabolic and morphological modulation within 30 days would provide novel preliminary insight into early-phase response dynamics [19-20].

Therefore, the present study was designed to evaluate the short-term safety and clinical effects of a multi-component nutraceutical formulation in women diagnosed with PCOS. Unlike previous single-ingredient trials, this investigation assessed metabolic (fasting blood glucose), morphological (antral follicle count and ovarian volume), neuroendocrine (serum cortisol), and quality-of-life outcomes concurrently over a 30-day supplementation period. The primary objective was to determine whether short-term supplementation would significantly improve fasting glucose levels, ovarian morphology, and cortisol concentration. Secondary objectives included assessment of quality-of-life outcomes and safety.

Materials

The investigational product used in this study was Miror PCOS Advanced Care Tablets, a multi-component nutraceutical formulation developed to support metabolic, endocrine, and stress-related pathways implicated in polycystic ovary syndrome (PCOS). The product was manufactured by Miror Therapeutics Private Limited, Bengaluru, India, a facility operating under Good Manufacturing Practice (GMP) certification in accordance with national regulatory standards. Manufacturing procedures adhered to standardized quality control protocols to ensure batch-to-batch consistency.

Each tablet contained a standardized blend of nutraceutical ingredients, including insulin-sensitizing compounds, antioxidant components, micronutrients, and botanical extracts known to influence metabolic regulation and oxidative balance. Raw materials were sourced from certified suppliers and subjected to identity testing prior to formulation. Finished batches were evaluated for uniformity of weight, disintegration time, microbial load, heavy metal content, and stability under controlled environmental conditions. Stability testing was conducted in accordance with International Council for Harmonisation (ICH) guidelines to ensure product integrity throughout the study period. The investigational product was supplied in sealed blister packaging and stored at controlled room temperature (25 ± 2°C, relative humidity 60 ± 5%) at the study site. Participants received identical packaging to maintain uniformity in administration.

The study was sponsored by Miror Therapeutics Private Limited, Bengaluru, India who provided the investigational product and logistical support. The sponsor did not participate in data analysis, statistical evaluation, or interpretation of results. Data integrity and analysis were maintained independently by the clinical research team. The clinical study was conducted at CCFT Laboratories, Meerut, India, a registered clinical research facility with established infrastructure for interventional studies. Laboratory investigations were performed at a NABL-accredited diagnostic laboratory, India ensuring compliance with national quality standards. Biochemical analyses, including fasting blood glucose and serum cortisol, were conducted using automated analyzers calibrated according to manufacturer specifications.

Transvaginal ultrasonographic evaluations were performed using a high-resolution ultrasound system (Siemens Healthineers) equipped with a 5–9 MHz transvaginal probe. All scans were conducted by a certified radiologist with experience in gynecological imaging. Ovarian volume was calculated using the standard ellipsoid formula (length × width × thickness × 0.523), and antral follicle count (AFC) was determined by counting follicles measuring 2–9 mm in diameter in each ovary.

METHODOLOGY:

Study Design and Regulatory Compliance

This investigation was designed as a prospective, open-label, single-arm, interventional clinical study conducted to evaluate the short-term safety and clinical effects of a multi-component nutraceutical formulation in women diagnosed with polycystic ovary syndrome (PCOS). The study was conducted under Protocol No. CTSRS/2521 and adhered to the ethical principles outlined in the Declaration of Helsinki (2013 revision) and the International Council for Harmonisation – Good Clinical Practice (ICH-GCP) guidelines.

Ethical approval was obtained from the Institutional Ethics Committee (IEC) prior to initiation of participant recruitment (IEC Approval No.: PDCEC/ SRS-03/ CTSRS/2521/10 Oct 25). Written informed consent was obtained from all participants before any study-related procedures were performed.

The study was conducted between 28-Oct-2025 and 07-Dec-2025 at CCFT Laboratories, Meerut, India, a registered clinical research facility equipped for interventional studies.

Participant Recruitment and Screening

Participants were recruited through outpatient gynecology clinics affiliated with the study site. Women aged 18–35 years presenting with symptoms suggestive of PCOS were screened for eligibility. Diagnosis of PCOS was established according to the Rotterdam criteria, requiring at least two of the following [22]:

1. Oligo- or anovulation
2. Clinical or biochemical hyperandrogenism
3. Polycystic ovarian morphology confirmed by transvaginal ultrasonography

Participants were excluded if they were pregnant or lactating, had thyroid dysfunction, Cushing's syndrome, diabetes mellitus requiring pharmacotherapy, hyperprolactinemia, or had used hormonal therapy or insulin-sensitizing agents within the preceding three months. Women with significant hepatic, renal, or cardiovascular disease were also excluded to minimize confounding metabolic influences. Eligible participants underwent baseline laboratory investigations and ultrasonographic assessment prior to enrolment.

Sample Size Consideration

A total of 40 participants were enrolled in this exploratory study. The sample size was determined based on feasibility and preliminary effect estimation objectives rather than formal power calculation, as the primary purpose was to generate short-term clinical evidence to inform future randomized controlled trials. Thirty-eight participants completed the study, resulting in a completion rate of 95%.

Intervention and Compliance Monitoring

Participants received one tablet of the investigational nutraceutical formulation daily for 30 consecutive days. The dosage regimen was selected based on manufacturer-recommended intake and safety evaluation data. Participants were instructed to maintain their usual dietary habits and physical activity patterns during the study period to reduce external variability. They were advised to avoid initiating new medications or supplements unless medically necessary. Compliance was assessed by tablet count at the end-of-study visit and review of participant-maintained daily intake diaries. Participants demonstrating compliance below 80% were to be excluded from per-protocol analysis; however, all completers met compliance criteria.

Study Visits and Assessments

Participants attended two primary study visits:

Visit 1 (Baseline, Day 0):

- Informed consent
- Demographic data collection
- Medical history
- Physical examination
- Measurement of vital signs
- Fasting blood sample collection
- Transvaginal ultrasonography
- Administration of WHOQOL-BREF questionnaire

Visit 2 (Day 30 ± 2 days):

- Repeat fasting blood sampling
- Repeat ultrasonography
- Re-administration of WHOQOL-BREF
- Adverse event assessment
- Compliance evaluation

Outcome Measures

Primary Outcomes

1. **Fasting Blood Glucose (FBG):**
   Venous blood samples were collected after an overnight fast of 8–10 hours. FBG was measured using an automated clinical chemistry analyzer calibrated according to manufacturer specifications.
2. **Ovarian Morphology:**
   Transvaginal ultrasonography was performed using a high-resolution ultrasound system equipped with a 5–9 MHz probe. Ovarian volume was calculated using the ellipsoid formula (length × width × thickness × 0.523). Antral follicle count (AFC) was determined by counting follicles measuring 2–9 mm in each ovary.
3. **Serum Cortisol:**
   Morning serum cortisol levels were measured using a standardized immunoassay method at the accredited laboratory. All samples were processed under controlled laboratory conditions to ensure analytical accuracy.

Secondary Outcomes

1. **Quality of Life Assessment:**
   The WHOQOL-BREF instrument was administered to evaluate physical, psychological, social, and environmental domains. Scores were calculated according to standardized scoring procedures.
2. **Subject Global Assessment (SGA):**
   Participants provided subjective evaluation of symptom improvement at the end of the study.
3. **Safety Monitoring:**
   Adverse events were recorded throughout the study. Vital signs were monitored at each visit. Laboratory abnormalities, if any, were documented.

Data Management and Statistical Analysis

All data were recorded in structured case report forms and subsequently entered into a secured electronic database. Data verification was conducted by cross-checking source documents to ensure accuracy and completeness. Continuous variables were expressed as mean ± standard deviation (SD). The Shapiro–Wilk test was used to assess normality of data distribution. Paired t-tests were employed to compare baseline and post-intervention values for normally distributed variables. A p-value < 0.05 was considered statistically significant. Statistical analyses were performed using IBM SPSS Statistics (v31.0.0). Both intention-to-treat and per-protocol analyses were explored; results presented reflect per-protocol findings due to minimal attrition.

Bias Control and Study Limitations

Given the open-label, single-arm design, blinding was not implemented. To reduce measurement bias, ultrasonographic evaluations were performed by the same experienced radiologist using standardized methodology. Laboratory analyses were conducted in an accredited facility to ensure analytical reliability. The absence of a control group limits causal inference. However, the short intervention duration and consistency of directional change across multiple endpoints support exploratory interpretation.

RESULTS AND DISCUSSION:

A total of 40 women diagnosed with PCOS were enrolled in the study, and 38 participants completed the 30-day intervention, yielding a completion rate of 95%. Two participants withdrew for personal reasons unrelated to the investigational product. No participant discontinued due to adverse effects, indicating good short-term tolerability. At baseline, the study population reflected a typical PCOS metabolic profile. The mean age was 26.37 ± 2.74 years, and the mean body mass index (BMI) was 22.60 ± 0.67 kg/m², consistent with overweight status commonly observed in PCOS cohorts. Baseline fasting blood glucose (FBG) values were in the upper-normal to impaired fasting range (104.53 ± 9.56 mg/dL), suggesting underlying insulin resistance in a substantial proportion of participants. Mean serum cortisol levels (19.94 ± 2.84 µg/dL) were within the upper physiological range, potentially reflecting stress-axis involvement. Baseline demographic and clinical characteristics, Change in Fasting Blood Glucose are summarized in Table 1 and 2. In, Fig-1 depicted reduction in fasting blood glucose after 30 Days.

Table 1. Baseline Demographic and Clinical Characteristics (n = 38).

Parameter	Mean ± SD
Age (years)	26.37 ± 2.74
Body Mass Index (kg/m²)	22.60 ± 0.67
Fasting Blood Glucose (mg/dL)	104.53 ± 9.56
Serum Cortisol (µg/dL)	19.94 ± 2.84

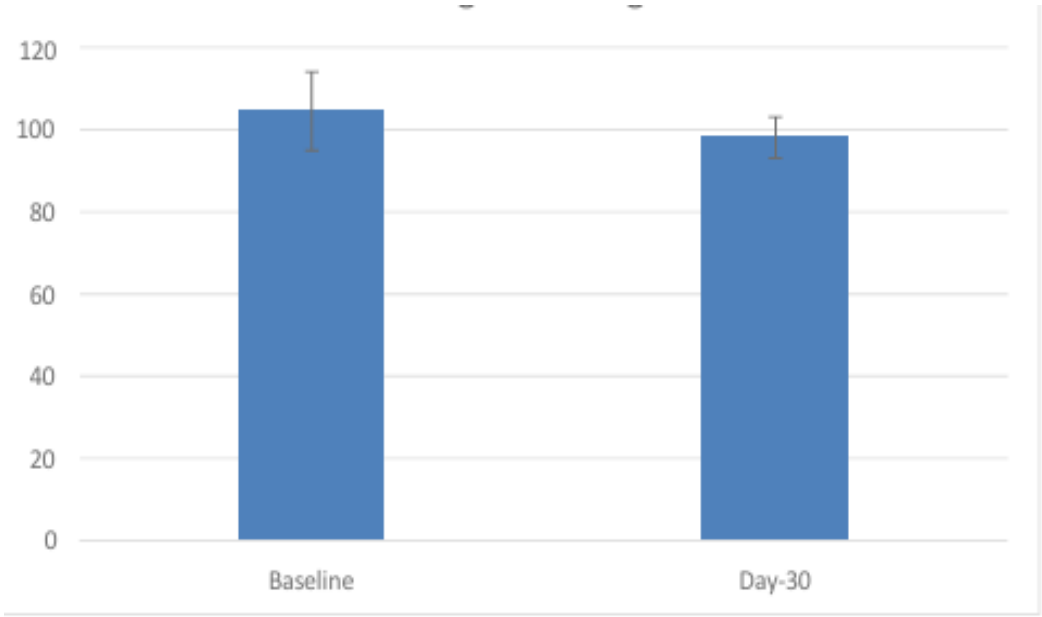

Figure 1. Reduction in Fasting Blood Glucose After 30 Days (Bar graph showing baseline vs Day 30 mean ± SD).

After 30 days of supplementation, a statistically significant reduction in fasting blood glucose was observed (98.06 ± 5.05 mg/dL; $p < 0.01$), representing a mean decrease of 6.47 mg/dL. Although modest, this reduction is clinically meaningful in women at risk for impaired glucose tolerance. The early metabolic response suggests potential improvement in insulin sensitivity. Previous randomized trials involving inositol supplementation have demonstrated reductions in fasting glucose and improved insulin sensitivity indices, typically over 8–12 weeks [23-25].

The present findings indicate that measurable glycemic modulation may occur within a shorter timeframe when multiple metabolic pathways are targeted simultaneously. Mechanistically, insulin-sensitizing components may enhance peripheral glucose uptake through improved receptor signaling, while antioxidant constituents may mitigate oxidative stress–induced impairment of insulin action.

Table 2. Change in Fasting Blood Glucose

Timepoint	Mean ± SD (mg/dL)	Mean Difference	p-value
Baseline	104.53 ± 9.56	—	—
Day 30	98.06 ± 5.05	-6.47 mg/dL	<0.01

In addition to metabolic improvements, significant changes were observed in ovarian morphology. Right ovarian volume decreased from 16.21 ± 9.09 cm^3 to 12.58 ± 9.48 cm^3 ($p < 0.01$), and left ovarian volume decreased from 14.30 ± 10.01 cm^3 to 11.78 ± 10.00 cm^3 ($p < 0.05$). Similarly, antral follicle count (AFC) declined bilaterally, with reductions of approximately four follicles in the right ovary and three follicles in the left ovary. These findings suggest potential modulation of follicular dynamics.

Table 3. Ovarian Volume and Antral Follicle Count

Parameter	Baseline	Day 30	p-value
Right Ovary Volume (cm^3)	16.21 ± 9.09	12.58 ± 9.48	<0.01
Left Ovary Volume (cm^3)	14.30 ± 10.01	11.78 ± 10.00	<0.05
Right AFC	16.77 ± 1.44	12.80 ± 1.95	<0.01
Left AFC	13.62 ± 2.36	10.65 ± 2.19	<0.05

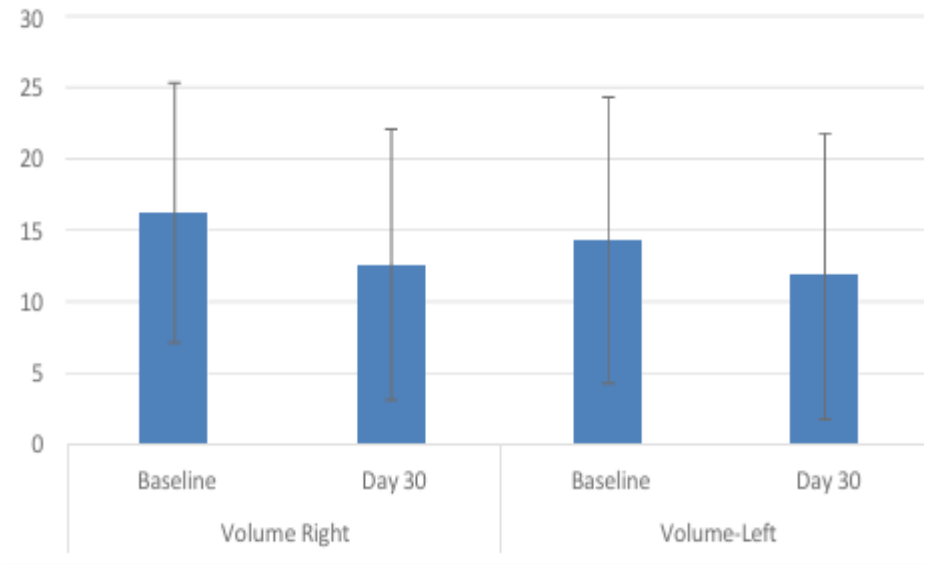

Figure 2. Percentage Reduction in Ovarian Volume and AFC (Clustered bar graph showing baseline vs Day 30 for right and left ovaries).

Morphological improvement within 30 days is noteworthy, as most nutraceutical studies focus predominantly on biochemical or hormonal markers without ultrasonographic evaluation. Insulin resistance and hyperinsulinemia promote ovarian androgen synthesis, contributing to follicular arrest. By improving insulin signaling, the intervention may have reduced intra-ovarian androgen exposure, facilitating improved follicular maturation and reduction of arrested follicles. While ovulatory outcomes were not directly assessed, the decrease in ovarian volume and AFC may reflect early normalization of ovarian microenvironment. Serum cortisol levels

demonstrated a significant reduction from 19.94 ± 2.84 µg/dL to 16.43 ± 2.33 µg/dL ($p < 0.01$). This decline suggests potential modulation of hypothalamic–pituitary–adrenal (HPA) axis activity. Elevated cortisol is associated with visceral adiposity and insulin resistance, and stress-related endocrine dysregulation has been increasingly implicated in PCOS pathophysiology. Few nutraceutical trials incorporate cortisol as an endpoint, making this observation a relatively novel contribution. Adaptogenic botanical components within the formulation may influence stress resilience and neuroendocrine balance. The observed reduction in cortisol may have contributed indirectly to improved metabolic parameters, highlighting a possible interaction between stress modulation and glycemic regulation.

Table 4. Serum Cortisol Levels

Timepoint	Mean ± SD (µg/dL)	Mean Difference	p-value
Baseline	19.94 ± 2.84	—	—
Day 30	16.43 ± 2.33	-3.51 µg/dL	<0.01

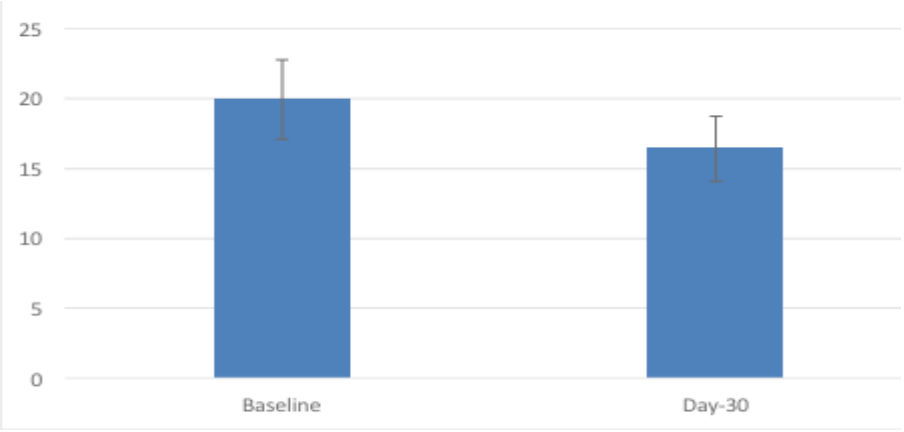

Figure 3. Reduction in Serum Cortisol After Supplementation (Bar graph baseline vs Day 30)

Quality-of-life outcomes also improved significantly across all WHOQOL-BREF domains, including physical, psychological, social, and environmental components ($p < 0.01$ for all domains). Women with PCOS frequently experience psychological distress, body image dissatisfaction, and reduced self-esteem. Improvements in metabolic stability and potential hormonal balance may positively influence psychological well-being. Additionally, reduction in stress biomarkers may contribute to perceived improvement in overall functioning. These findings emphasize the importance of integrating patient-reported outcomes alongside biochemical measures when evaluating nutraceutical interventions.

Table 5. WHOQOL-BREF Domain Scores.

Domain	Baseline	Day 30	p-value
Physical	44±5.4	94± 5.4	<0.01
Psychological	38 ± 5.8	88 ± 6.1	<0.01
Social Relationships	44 ± 7.0	94 ± 6.5	<0.01
Environmental	50 ± 6.8	75 ± 5.9	<0.01

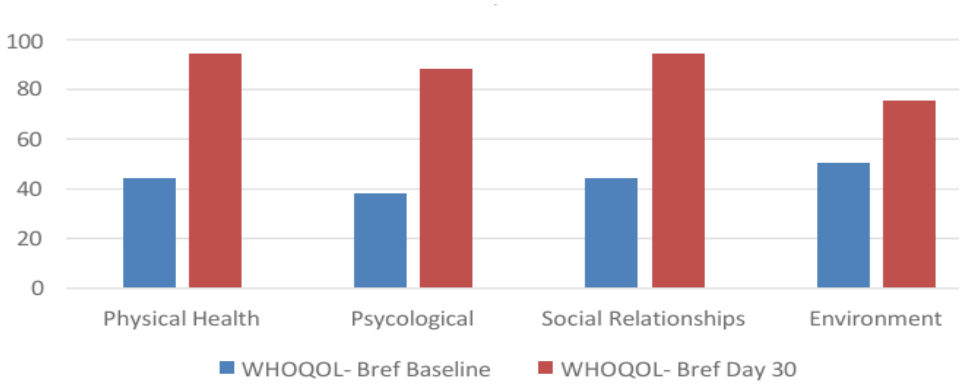

Figure 4. Improvement in WHOQOL-BREF Domains (Line graph showing increase across domains)

Importantly, the direction of change across metabolic, morphological, neuroendocrine, and quality-of-life domains was consistent. Such convergence across multiple endpoints strengthens the biological plausibility of the findings. While the open-label, single-arm design limits causal inference, the uniformity of improvement across diverse physiological systems suggests that multi-target nutraceutical strategies warrant further exploration. Safety analysis revealed no serious adverse events during the study period. Mild gastrointestinal discomfort was reported in two participants and resolved spontaneously without discontinuation. Vital signs remained stable throughout the intervention. The favorable tolerability profile supports the short-term safety of the formulation. When compared with previous nutraceutical trials in PCOS, several distinguishing features emerge. Most published studies evaluate single ingredients such as myo-inositol, curcumin, omega-3 fatty acids, or vitamin D in isolation. Although beneficial effects have been documented, PCOS is a multifactorial condition involving intertwined metabolic, inflammatory, and neuroendocrine pathways. The present study assessed an integrated multi-component formulation designed to target multiple mechanisms concurrently. Additionally, inclusion of ultrasonographic parameters and cortisol measurement expands the evaluative scope beyond conventional glycemic or hormonal endpoints.

Nevertheless, interpretation must remain cautious. The absence of a placebo control group introduces potential expectation bias. The short duration limits assessment of sustained efficacy and reproductive outcomes. Future randomized controlled trials with larger sample sizes and longer follow-up are necessary to confirm these preliminary findings and determine long-term clinical relevance.

CONCLUSION:

In conclusion, this pilot study provides encouraging preliminary evidence that a rationally designed multi-component nutraceutical formulation may offer short-term benefits for metabolic parameters, ovarian morphology, stress biomarkers, and quality of life in women with PCOS. While these results are promising, they should be interpreted cautiously given the study's methodological limitations. Rigorous randomized controlled trials are essential to confirm these findings, establish optimal dosing regimens, and determine the formulation's place within the therapeutic armamentarium for PCOS management. If validated, such nutraceutical interventions could represent safe, accessible, and patient-centered additions to the multidisciplinary care of women with this complex and prevalent endocrine disorder.

Acknowledgements

The authors thank all participants for their involvement in the study. The support of the clinical staff, laboratory personnel, and radiology team at CCFT Laboratories, Meerut in conducting assessments and data collection is gratefully acknowledged.

Funding Source

This study was supported by Miror Therapeutics Private Limited, Bangaluru, India, who provided the investigational product and logistical assistance.

REFERENCES:

1. Helena J Teede, Marie L Misso, Michael F Costello, Anuja Dokras, Joop Laven, Lisa Moran, Terhi Piltonen, Robert J Norman, International PCOS Network , Recommendations from the international evidence-based guideline for the assessment and management of polycystic ovary syndrome, Human Reproduction, Volume 33, Issue 9, September 2018, Pages 1602–1618, https://doi.org/10.1093/humrep/dey256.
2. Fitz, V., Graca, S., Mahalingaiah, S., Liu, J., Lai, L., Butt, A., … Teede, H. (2024). Inositol for polycystic ovary syndrome: A systematic review and meta-analysis to inform the 2023 international evidence-based PCOS guidelines. Journal of Clinical Endocrinology & Metabolism, 109(6), 1630–1655. https://doi.org/10.1210/clinem/dgad762.
3. Greff, D., Juhász, A. E., Váncsa, S., Váradi, A., Sipos, Z., Szinte, J., Horváth, E. M. (2023). *Inositol is an effective and safe treatment in polycystic ovary syndrome: A systematic review and meta-analysis of randomized controlled trials*. Reproductive Biology and Endocrinology, 21, 10. https://doi.org/10.1186/s12958-023-01055-z.
4. Zhao, G., Fan, Y., Li, R., Huang, Y., Li, W., Zhao, Y., & Zhou, M. (2025). *The effectiveness of nutritional supplements in improving polycystic ovary syndrome in women: A systematic review and network meta-analysis*. Reproductive Biology and Endocrinology, 23, 94. https://doi.org/10.1186/s12958-025-01409-9
5. Moslehi, N., Zeraattalab-Motlagh, S., Rahimi Sakak, F., Shab-Bidar, S., & Ramezani Tehrani, F. (2023). *Effects of nutrition on metabolic and endocrine outcomes in women with polycystic ovary syndrome: An umbrella review of meta-analyses*. Nutrition Reviews, 81(5), 555–577. https://doi.org/10.1093/nutrit/nuac075
6. Abdelazeem, B., Abbas, K. S., Shehata, J., Baral, N., Banour, S., & Hassan, M. (2022). *The effects of curcumin as dietary supplement for patients with polycystic ovary syndrome: An*

updated systematic review and meta-analysis. Phytotherapy Research, 36(1), 22–32. https://doi.org/10.1002/ptr.7274

7. Feghhi, F., Ghaznavi, H., Sheervalilou, R., Razavi, M., & Sepidarkish, M. (2024). *Effects of metformin and curcumin in women with polycystic ovary syndrome: A factorial clinical trial*. Phytomedicine. https://doi.org/10.1016/j.phymed.2024.156160
8. Bahramian, H., Sherafatmanesh, S., Asadi, N., Bakhshi, A., & Eftekhari, M. H. (2023). *Effects of single-dose and co-supplementation of vitamin D and omega-3 on metabolic profile in women with polycystic ovary syndrome: A randomized clinical trial*. International Journal of Reproductive Biomedicine, 21(7), 541–550. https://doi.org/10.18502/ijrm.v21i7.13889
9. Albardan, L., Platat, C., & Kalupahana, N. S. (2024). *Role of omega-3 fatty acids in improving metabolic dysfunctions in polycystic ovary syndrome*. Nutrients, 16(17), 2961. https://doi.org/10.3390/nu16172961
10. Melo, V., Silva, T., Silva, T., Freitas, J., Sacramento, J., & Vazquez, M. (2022). *Omega-3 supplementation in the treatment of polycystic ovary syndrome (PCOS): A review of clinical trials and cohort studies*. Endocrine Regulations, 56(1), 66–79. https://doi.org/10.2478/enr-2022-0008
11. Teede, H. J., Joham, A. E., Paul, E., et al. (2018). *International evidence-based guideline for the assessment and management of polycystic ovary syndrome*. Human Reproduction, 33(9), 1602–1618. https://doi.org/10.1093/humrep/dey256
12. Katyal, G., Kaur, G., Ashraf, H., Bodapati, A., Hanif, A., Okafor, D. K., & Khan, S. (2024). *Systematic review of the roles of inositol and vitamin D in improving fertility among patients with polycystic ovary syndrome*. Clinical and Experimental Reproductive Medicine, 51(3), 181–191. https://doi.org/10.5653/cerm.2023.06485
13. Menichini, D., Ughetti, C., Monari, F., Di Vinci, P. L., Neri, I., & Facchinetti, F. (2022). *Nutraceuticals and polycystic ovary syndrome: A systematic review of the literature*. Gynecological Endocrinology, 38(8), 623–631. https://doi.org/10.1080/09513590.2022.2089106
14. Moslehi, N., Sakak, F. R., & Mirmiran, P. (2023). *Effects of nutrition on metabolic and endocrine outcomes in women with PCOS: An umbrella review of RCT meta-analyses*. Nutrition Reviews, 81, 555–577. https://doi.org/10.1093/nutrit/nuac075
15. Mallya, P., & Lewis, S. A. (2025). *Curcumin and its formulations for the treatment of polycystic ovary syndrome: Current insights and future prospects*. Journal of Ovarian Research, 18, 78. https://doi.org/10.1186/s13048-025-01660-z
16. Abdelazeem, B., & Baral, N. (2022). *The effects of curcumin as dietary supplement for patients with PCOS: Meta-analysis of randomized clinical trials*. Phytotherapy Research, 36(1), 22–32. https://doi.org/10.1002/ptr.7274
17. Greff, D., et al. (2023). *Inositol is effective and safe for PCOS: Meta-analysis of RCTs*. Reproductive Biology and Endocrinology, 21, 10. https://doi.org/10.1186/s12958-023-01055-z
18. Fitz, V., et al. (2024). *Inositol meta-analysis for 2023 guidelines*. Journal of Clinical Endocrinology & Metabolism, 109(6), 1630–1655. https://doi.org/10.1210/clinem/dgad762
19. Zhao, G., et al. (2025). *Nutritional supplements meta-analysis in PCOS*. Reproductive Biology and Endocrinology, 23, 94. https://doi.org/10.1186/s12958-025-01409-9
20. Albardan, L., et al. (2024). *Omega-3 role in metabolic dysfunctions in PCOS*. Nutrients, 16(17), 2961. https://doi.org/10.3390/nu16172961
21. Bahramian, H., et al. (2023). *Vitamin D + omega-3 co-supplementation RCT in PCOS*. International Journal of Reproductive Biomedicine, 21(7), 541–550. https://doi.org/10.18502/ijrm.v21i7.13889.
22. Helena J Teede, Marie L Misso, Michael F Costello, Anuja Dokras, Joop Laven, Lisa Moran, Terhi Piltonen, Robert J Norman, International PCOS Network , Recommendations from the international evidence-based guideline for the assessment and management of polycystic ovary syndrome, Human Reproduction, Volume 33, Issue 9, September 2018, Pages 1602–1618, https://doi.org/10.1093/humrep/dey256.
23. Genazzani AD, Prati A, Santagni S, et al. Differential insulin response to myo-inositol administration in obese PCOS patients. Gynecological Endocrinology. 2012;28(12):969–973. DOI: https://doi.org/10.3109/09513590.2012.685205
24. Cooney LG, Lee I, Sammel MD, Dokras A. (2017). High prevalence of moderate and severe depressive and anxiety symptoms in polycystic ovary syndrome: A systematic review and meta-analysis. Human Reproduction. 32(5):1075–1091. https://doi.org/10.1093/humrep/dex044.
25. Pundir J, Psaroudakis D, Savnur P, et al. Inositol treatment of anovulation in women with polycystic ovary syndrome: a meta-analysis of randomised trials. BJOG. 2018;125(3):299–308. DOI: https://doi.org/10.1111/1471-0528.14754.