

Effects of Functional Training and Berberine Supplementation on Androgen Hormones in Women with Polycystic Ovary Syndrome (PCOS)

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Abstract

Introduction: Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders among women and is characterized by hyperandrogenism, infertility, and insulin resistance. This study aimed to investigate the effects of 12 weeks of functional training combined with berberine supplementation on sexual and metabolic hormones in women with PCOS.

Methods: In a randomized controlled trial, forty women with PCOS (aged 20–35 years) were randomly assigned to four groups: control, exercise, berberine, and exercise + berberine. The functional training protocol consisted of multi-joint movements performed three 60-minute sessions per week for 12 weeks. Participants in the berberine groups received two 500 mg tablets daily. Serum levels of testosterone, DHEA, PRL, LH, FSH, SHBG, estrogen, progesterone, and TSH were measured before and after the intervention using the ELISA method. Data were analyzed using paired t-tests and ANCOVA with a significance level set at $p < 0.05$.

Results: After 12 weeks, significant reductions were observed in testosterone ($p = 0.001$, $\eta^2 = 0.42$) and DHEA ($p = 0.02$, $\eta^2 = 0.28$) in the intervention groups. Prolactin levels also decreased significantly ($p = 0.015$), whereas SHBG levels increased ($p = 0.04$). Changes in LH, FSH, progesterone, and TSH were not statistically significant ($p > 0.05$). Overall, the combined intervention of functional training and berberine supplementation produced greater improvements than either intervention alone.

Conclusions: The combination of functional exercise and berberine supplementation improved hormonal profiles and reduced androgen levels in women with PCOS. These findings suggest that integrated non-pharmacological approaches may serve as effective and safe strategies for managing PCOS symptoms.

Key Words: Polycystic ovary syndrome (PCOS); Functional training; Berberine; Androgenic hormones.

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1. Introduction

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders affecting women of reproductive age and is characterized by hyperandrogenism, amenorrhea or oligomenorrhea, and polycystic ovarian morphology [1]. The prevalence of PCOS is estimated to range from 6% to 20% among women of reproductive age, making it one of the leading causes of anovulatory infertility worldwide [2]. In addition to reproductive dysfunction, PCOS is associated with several metabolic abnormalities, including insulin resistance, hyperglycemia, dyslipidemia, and central obesity, all of which contribute to an increased risk of developing type 2 diabetes mellitus and cardiovascular diseases [3].

Although the exact etiology of PCOS has not yet been fully elucidated, accumulating evidence suggests that its pathogenesis involves a complex interaction among genetic, environmental, and metabolic factors. Insulin resistance is considered one of the key mechanisms underlying the syndrome, resulting in compensatory hyperinsulinemia that stimulates excessive ovarian androgen production [2]. Furthermore, chronic low-grade inflammation and genetic predisposition have been identified as important contributors to the development of the disorder [3]. The clinical manifestations of PCOS are heterogeneous and include ovulatory dysfunction, hirsutism, acne, androgenic alopecia, central obesity, infertility, and, in some cases, psychological disturbances such as anxiety and depression [4]. The diagnosis of PCOS is primarily based on internationally accepted criteria, particularly the Rotterdam criteria, which require the presence of at least two of the following three features: oligo-/anovulation, clinical or biochemical hyperandrogenism, and polycystic ovarian morphology on ultrasonography [5].

From a clinical perspective, PCOS extends beyond a reproductive disorder and is increasingly recognized as a complex metabolic syndrome associated with an elevated risk of type 2 diabetes mellitus, metabolic syndrome, cardiovascular disease, and endometrial cancer [6,7]. Moreover, the physical manifestations of hyperandrogenism and infertility often impose substantial psychological burdens, including diminished self-esteem and an increased

prevalence of anxiety and depressive disorders. Although no definitive cure for PCOS currently exists, lifestyle modification, weight management, regular physical activity, and pharmacological interventions such as metformin and ovulation-inducing agents have been shown to effectively alleviate its clinical manifestations and reduce long-term complications [8]. Epidemiological evidence indicates that PCOS affects approximately 6–13% of women of reproductive age worldwide, while several meta-analyses have reported an overall prevalence of approximately 9.2%. Given its high prevalence and its broad reproductive, metabolic, and psychological consequences, PCOS is now regarded as a major global public health challenge.

In recent years, increasing attention has been directed toward lifestyle modification, particularly dietary management and regular physical activity, as fundamental components of PCOS management [4]. Regular exercise, especially combined or functional training, has been shown to improve insulin sensitivity, reduce body mass index (BMI), and decrease circulating free androgen levels [5]. Consequently, exercise-induced improvements in metabolic health are considered among the most effective non-pharmacological strategies for managing PCOS. Alongside exercise interventions, natural compounds and herbal supplements have also gained considerable interest as complementary therapeutic approaches. Berberine, an isoquinoline alkaloid with well-documented antidiabetic and anti-inflammatory properties, has demonstrated beneficial effects on glucose and lipid metabolism in numerous clinical and experimental studies [6]. The primary mechanism of action of berberine involves activation of the AMP-activated protein kinase (AMPK) signaling pathway, which enhances glucose uptake, improves insulin sensitivity, and promotes fatty acid oxidation [7]. In addition, accumulating evidence suggests that berberine may reduce circulating androgen levels and improve ovarian function in women with PCOS [8].

Because both functional exercise and berberine supplementation have independently demonstrated beneficial effects on the metabolic and hormonal disturbances associated with PCOS, combining these interventions may produce synergistic therapeutic effects. Functional training, which incorporates multi-joint, integrated movement patterns designed to

improve muscular strength, balance, coordination, and functional performance, enhances insulin sensitivity by increasing skeletal muscle glucose utilization and improving body composition [9]. Simultaneously, berberine may further potentiate these benefits through its anti-inflammatory actions and regulation of key metabolic signaling pathways. Despite these promising findings, evidence regarding the combined effects of functional training and berberine supplementation on hormonal profiles in women with PCOS remains limited. Given the multifactorial nature of PCOS, which involves complex interactions among genetic, environmental, metabolic, and endocrine factors, investigating multimodal non-pharmacological interventions may provide valuable insights into optimizing disease management.

Therefore, the present study aimed to investigate the effects of a 12-week functional training program combined with berberine supplementation on sex hormone and metabolic profiles in women with polycystic ovary syndrome.

2. Methods

2.1. Participants

The study population consisted of women aged 20–35 years who had been diagnosed with polycystic ovary syndrome (PCOS) according to the 2003 Rotterdam criteria, which require the presence of at least two of the following three diagnostic features: (1) oligomenorrhea or amenorrhea, (2) clinical and/or biochemical hyperandrogenism, and (3) polycystic ovarian morphology confirmed by ultrasonography. Participants were excluded if they had metabolic or cardiovascular diseases, were taking medications known to affect ovarian function, were pregnant, or were unwilling to continue participation during the study. A total of 40 eligible participants were enrolled, with a mean age of 27.4 ± 3.8 years and a mean body mass index (BMI) of 28.6 ± 3.2 kg/m².

2.2. Study design

This study was conducted as a randomized controlled trial (RCT) with a parallel-group design. Following enrollment, the 40 participants were randomly assigned using a simple randomization procedure to one of four groups ($n = 10$ per group): Control, Functional Training (FT), Berberine (BBR), and

Functional Training plus Berberine (FT+BBR). The intervention was carried out over a period of 12 weeks. The study was performed in accordance with the principles of the Declaration of Helsinki, and written informed consent was obtained from all participants before enrollment. Fasting venous blood samples were collected at 8:00 a.m. before and after the 12-week intervention for biochemical assessments.

2.3. Sample size calculation

The provided text does not report a formal a priori sample size calculation. The sample size was determined based on the number of eligible participants who met the inclusion criteria and were successfully recruited for the study, resulting in a final sample of 40 participants, with 10 participants allocated to each of the four intervention groups.

2.4. Nutritional intervention / Supplementation protocol

Participants assigned to the Berberine (BBR) and Functional Training plus Berberine (FT+BBR) groups received two 500-mg berberine tablets daily, equating to a total daily dose of 1,000 mg, for 12 consecutive weeks. The supplement was administered after the main meals. Adherence to the supplementation protocol was monitored through weekly telephone follow-up and via compliance records completed by the participants.

2.5. Exercise protocol

Participants in the Functional Training (FT) and FT+BBR groups completed a supervised 12-week functional training program consisting of three sessions per week, with each session lasting 60 minutes. Exercise intensity was maintained at a rating of perceived exertion (RPE) of 13–16 according to the Borg Scale. Each training session consisted of three phases: a 10-minute general and specific warm-up, a 40-minute main exercise session, and a 10-minute cool-down with stretching exercises. The main exercise program included multi-joint functional movements such as squats, lunges, planks, push-ups, jump rope exercises, and plyometric drills. All training sessions were performed in groups under the supervision of a certified exercise physiologist.

2.7. Dietary control and physical activity standardization

The provided text does not specify any formal dietary control measures or standardization of physical activity outside of the prescribed intervention. Participants were not subjected to a controlled diet, nor is there mention of monitoring or restricting their habitual physical activity levels during the 12-week study period.

2.8. Statistical analysis

All statistical analyses were performed using IBM SPSS Statistics software (Version 24.0; IBM Corp., Armonk, NY, USA). The normality of data distribution was assessed using the Shapiro–Wilk test, while the homogeneity of variances was evaluated using Levene's test. Within-group comparisons (pre- to post-intervention) were conducted using paired-samples *t*-tests, whereas between-group differences were analyzed using analysis of covariance (ANCOVA), with baseline values included as covariates to control for initial differences. Statistical significance was established at $*p < 0.05$ for all analyses. In addition, effect sizes were calculated and reported as partial eta squared (η^2) to assess the magnitude of the intervention effects.

3. Results

3.1. Participants' characteristics and compliance

A total of 40 participants ($n = 10$ per group) completed the 12-week intervention. As shown in Table 1, baseline demographic and anthropometric characteristics, including age, height, body weight, and body mass index (BMI), were comparable across the four study groups (Control, FT, BBR, and FT+BBR). No statistically significant differences were observed among the groups at baseline ($*p > 0.05$ for all comparisons), confirming the homogeneity of the sample and supporting the validity of subsequent between-group analyses.

3.2. Primary outcomes

The primary outcomes of this study were defined as changes in serum testosterone, dehydroepiandrosterone (DHEA), and sex hormone-binding globulin (SHBG) levels, which are key markers of hyperandrogenism in PCOS.

As presented in Table 2, within-group comparisons revealed that the combined intervention (FT+BBR)

led to a statistically significant reduction in testosterone levels (from 1.85 ± 0.42 to 1.30 ± 0.35 ng/mL; $*p = 0.001$), with a large effect size ($\eta^2 = 0.42$). Similarly, DHEA levels decreased significantly (from 2.60 ± 0.75 to 2.10 ± 0.60 µg/mL; $*p = 0.020$; $\eta^2 = 0.28$). In contrast, SHBG levels showed a significant increase (from 35.4 ± 6.8 to 39.7 ± 7.2 nmol/L; $*p = 0.040$; $\eta^2 = 0.20$).

3.3. Secondary outcomes

Secondary outcomes included changes in prolactin (PRL), estrogen, luteinizing hormone (LH), follicle-stimulating hormone (FSH), progesterone, and thyroid-stimulating hormone (TSH).

Within-group analysis (Table 2) demonstrated a significant reduction in prolactin levels (from 16.2 ± 3.5 to 13.9 ± 3.1 ng/mL; $*p = 0.015$; $\eta^2 = 0.25$) and a significant increase in estrogen levels (from 110 ± 25 to 125 ± 28 pg/mL; $*p = 0.030$; $\eta^2 = 0.22$) following the intervention. However, no significant changes were observed for LH ($p = 0.540$), FSH ($p = 0.070$), progesterone ($p = 0.620$), or TSH ($p = 0.480$). (Figure 1 visually depicts these changes, confirming that the intervention exerted selective effects on androgenic and estrogenic pathways rather than broadly affecting the hypothalamic–pituitary–ovarian (HPO) axis.

Figure 1. Comparison of Hormonal Levels Before and After the Intervention

*)Data are presented as mean $\pm$ SD; $*p < 0.05$; $*p < 0.01$; η^2 indicates effect size).

Between-group comparisons (Table 3) further revealed statistically significant differences across groups for prolactin ($F = 3.25$, $*p = 0.028$). For estrogen, the between-group difference approached statistical significance ($F = 2.75$, $*p = 0.050$). In contrast, no significant between-group differences were detected for LH, FSH, progesterone, or TSH ($F < 2$, $*p > 0.05$ for all), indicating that these parameters remained largely unaffected by the interventions.

Sample table

Table 1. Demographic Characteristics of Participants Across the Four Study Groups (Mean $\pm$ Standard Deviation)

p.value	FT+BBR	BBR	FT	Control	Variable
0.91	27.3 $\pm$ 3.6	27.2 $\pm$ 4.0	27.6 $\pm$ 3.5	27.4 $\pm$ 3.8	Age (years)
0.87	164 $\pm$ 6	165 $\pm$ 5	163 $\pm$ 6	164 $\pm$ 5	Height (cm)
0.88	75.2 $\pm$ 6.6	76.0 $\pm$ 7.1	74.5 $\pm$ 6.8	75.8 $\pm$ 6.4	Weight (kg)
0.92	28.6 $\pm$ 3.1	28.8 $\pm$ 3.5	28.5 $\pm$ 3.0	28.7 $\pm$ 3.2	BMI (kg/m ²)

Abbreviations: FT, Functional Training; BBR, Berberine; BMI, body mass index.

Regarding compliance, adherence to the supplementation protocol (for the BBR and FT+BBR groups) was monitored via weekly telephone follow-up and participant-completed compliance records. The reported adherence rate was high, with no major dropouts or adverse events reported during the study period. Similarly, participants in the FT and FT+BBR groups attended all supervised training sessions as scheduled.

Table 2. Within-Group Comparison of Hormonal Levels Before and After the 12-Week Intervention (FT+BBR Group)

Result	Effect Size (η^2)	*p*-value	Post-Intervention (Mean $\pm$ SD)	Pre-Intervention (Mean $\pm$ SD)	Variable
Significant decrease	0.42	0.001**	1.30 $\pm$ 0.35	1.85 $\pm$ 0.42	Testosterone (ng/mL)
Significant decrease	0.28	0.020*	2.10 $\pm$ 0.60	2.60 $\pm$ 0.75	DHEA (μg/mL)
Significant increase	0.20	0.040*	39.7 $\pm$ 7.2	35.4 $\pm$ 6.8	SHBG (nmol/L)

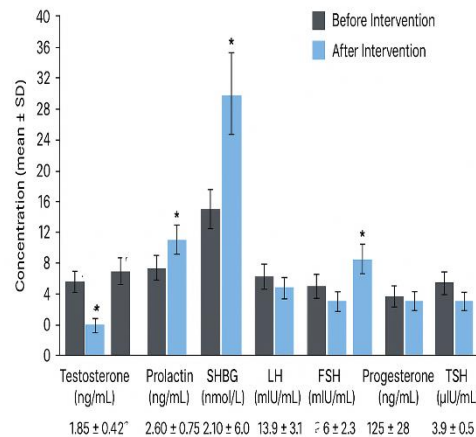
Furthermore, between-group comparisons using ANCOVA (Table 3) confirmed statistically significant differences across the four groups for testosterone ($F = 8.45$, $*p* = 0.001$), DHEA ($F = 4.38$, $*p* = 0.010$), and SHBG ($F = 2.90$, $*p* = 0.045$). The greatest reduction in testosterone was observed in the combined intervention group (FT+BBR), suggesting a synergistic effect of functional training and berberine supplementation.

Table 3. Between-Group Comparisons of Hormonal Changes After the 12-Week Intervention (ANCOVA)

Result	*p*-value	F-value	Variable
Significant difference between groups	0.001**	8.45	Testosterone
Significant difference	0.010*	4.38	DHEA
Significant difference	0.028*	3.25	Prolactin
Significant difference	0.045*	2.90	SHBG
Near-significant	0.050	2.75	Estrogen
Non-significant difference	> 0.05	< 2	LH, FSH, Progesterone, TSH

In summary, the results indicate that the 12-week functional training program combined with berberine supplementation significantly improved key androgen-related parameters (testosterone, DHEA, and SHBG) and favorably influenced prolactin and estrogen levels, while no significant effects were observed on gonadotropins, progesterone, or thyroid function. The combined intervention demonstrated the most pronounced benefits, suggesting a potential synergistic therapeutic effect for managing hormonal disturbances in women with PCOS.

Figure 1. Comparison of Hormonal Levels Before and After the Intervention



As shown in Figure 1, changes in serum hormone levels were observed before and after the intervention. Data are presented as mean $\pm$ standard deviation (SD). $p < 0.05$; $p < 0.01$. η^2 indicates effect size. Significant reductions were observed in testosterone, DHEA, and prolactin levels, whereas significant increases were found in SHBG and estrogen levels. No significant changes were observed in LH, FSH, progesterone, or TSH.

4. Discussion

The results of the present study indicate that a 12-week combined intervention of functional training and berberine supplementation exerts synergistic effects on metabolic and hormonal pathways in women with polycystic ovary syndrome (PCOS). The findings demonstrated significant reductions in testosterone and DHEA levels, alongside increases in SHBG and estrogen concentrations, particularly in the combined intervention group. These changes were not observed to the same extent in the monotherapy or control groups, suggesting a clear interaction between exercise-induced metabolic adaptations and the pharmacological actions of berberine.

The significant reductions in androgenic hormones observed in the combined group are consistent with previous research. Wei et al. [6] reported that berberine supplementation reduces androgen levels and improves insulin sensitivity in women with PCOS, likely through activation of the AMP-activated protein kinase (AMPK) pathway, which enhances glucose uptake and regulates lipid and carbohydrate metabolism [7,8]. Similarly, our exercise findings align with those of Patten et al. [1] and Shele et al. [2], who demonstrated that combined and resistance training reduce androgenic markers and improve insulin sensitivity in PCOS populations. The functional training protocol used in this study, incorporating multi-joint exercises such as squats, lunges, planks, and plyometric drills, likely contributed to improved body composition, increased lean muscle mass, and reduced visceral fat, all of which are known to enhance insulin sensitivity [9].

The observed increase in SHBG further reflects improved metabolic status, as reduced insulin

resistance is typically associated with increased hepatic SHBG synthesis. Likewise, the elevation in estrogen levels may indicate partial restoration of follicular function and improved estrogen–androgen balance [5]. These findings are mechanistically supported by the work of Sabag et al. [3], who showed that regular moderate-to-high intensity physical activity can modulate the hypothalamic–pituitary–ovarian (HPO) axis by reducing insulin levels and improving metabolic signaling pathways.

The lack of significant changes in LH, FSH, progesterone, and TSH suggests that the intervention primarily influenced metabolic and androgenic pathways rather than broadly affecting the HPO axis or thyroid function. This may be attributed to the relatively short intervention duration (12 weeks) or individual variability in menstrual cycle phases, which could have masked subtle effects on gonadotropins. From a clinical perspective, the reductions in androgens are noteworthy, as they may contribute to improvements in acne, hirsutism, menstrual irregularities, and infertility. Therefore, the combination of functional training and berberine supplementation may represent a safe, cost-effective, and non-pharmacological therapeutic strategy for women with PCOS, particularly in cases where pharmacological treatments are limited or contraindicated. However, the study has limitations, including a relatively small sample size ($n = 40$), a short intervention period, and the lack of strict control over dietary intake and menstrual cycle phase, which may have influenced hormonal outcomes. Future research with larger sample sizes, longer durations, and controlled dietary protocols is warranted to confirm these findings.

5. Conclusion

Polycystic ovary syndrome (PCOS) is a prevalent hormonal disorder in reproductive-aged women, characterized by hyperandrogenism, ovulatory dysfunction, and metabolic disturbances. This study investigated the effects of a 12-week functional training program combined with berberine supplementation on sex hormone and metabolic profiles in women with PCOS. The results demonstrated that the combined intervention significantly reduced testosterone, DHEA, and prolactin levels, while increasing SHBG and estrogen concentrations. No significant changes were observed in LH, FSH, progesterone, or TSH. The greatest improvements were seen in the combined intervention group, indicating a synergistic effect of exercise and berberine. Exercise enhances insulin sensitivity and metabolic function, while berberine activates the AMPK pathway and exerts anti-inflammatory effects. Together, these mechanisms contribute to reduced androgen production and improved hormonal balance. These findings support the integration of structured functional exercise with berberine supplementation as an effective complementary strategy for managing PCOS-related hormonal disturbances. Given the safety, cost-effectiveness, and accessibility of these interventions, they may be recommended as part of a comprehensive management approach for women with PCOS, especially when pharmacological options are limited. Further studies with larger sample sizes and longer follow-up periods are needed to validate these results and explore long-term clinical outcomes.

6. Highlights

Study Design: A 12-week randomized controlled trial (RCT) with four parallel groups (Control, Functional Training [FT], Berberine [BBR], and FT+BBR) was conducted in 40 women with PCOS (aged 20–35 years, BMI 28.6 ± 3.2 kg/m²).

Interventions: Functional training consisted of three weekly supervised sessions (60 min each, RPE 13–16) including multi-joint exercises (squats, lunges, planks, plyometrics). Berberine was administered at a daily dose of 1,000 mg (two 500-mg tablets after meals).

Key Findings: The combined FT+BBR intervention significantly reduced testosterone ($p = 0.001$, $\eta^2 = 0.42$) and DHEA ($p = 0.002$, $\eta^2 = 0.28$), increased SHBG ($p = 0.04$) and estrogen ($p = 0.03$), and decreased prolactin ($p = 0.05$). No significant changes were observed in LH, FSH, progesterone, or TSH.

Synergistic Effect: The combined group showed superior improvements compared to monotherapy groups, suggesting a synergistic interaction between exercise-induced metabolic adaptations and berberine's AMPK-mediated pharmacological effects.

Clinical Implications: This non-pharmacological combined strategy may be a safe, cost-effective, and accessible complementary approach for improving hormonal imbalances and androgen-related symptoms (e.g., hirsutism, menstrual irregularities) in women with PCOS.

Limitations: Small sample size ($n = 40$), short intervention duration (12 weeks), lack of dietary control, and no adjustment for menstrual cycle phase, which may affect hormonal measurements. Future studies should address these limitations with larger cohorts and extended follow-up.

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Conflicts of Interest

The authors declare that there are no conflicts of interest, whether financial, personal, scientific, or organizational, related to the conduct of this study, data analysis, or publication of the findings.

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