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Efficacy and Safety of Shatavari (Asparagus Racemosus) Root Extract in the Management of Menopausal Symptoms: A Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial

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ABSTRACT:

Introduction: Menopause is associated with vasomotor, psychological, and somatic symptoms that impair quality of life. The objectives was to evaluate the safety and efficacy of Shatavari root extract capsule improving menopause related hormonal changes and alleviating hot flushes and other climacteric symptoms.

Methods: Multicenter, randomized, double-blind, placebo-controlled trial enrolled 70 peri- and postmenopausal women, who randomized to receive Shatavari root extract capsules (400 mg/day) or placebo for 56 days. The primary objective was to evaluate effects on hot flushes and other climacteric symptoms compared with placebo. The secondary objective was to assess effects on stress, sleep, mood, quality of life, safety and tolerability.

Results: Baseline characteristics were comparable between groups. Shatavari significantly reduced menopausal symptoms (total MRS and somatic scores), improved quality of life (MENQOL) (total and psychosocial scores) and mood (total mood, tension-anxiety, vigor-activity scores) from Day 14 compared to placebo. Significant reduction in hot flush severity, other climacteric symptoms, stress, MENQOL, mood and improvement in sleep quality observed from Day 28. Shatavari significantly modulated serum estradiol (increased) and luteinizing hormone (decreased) from Day 14 and decreased cortisol from Day 42 compared to placebo. Follicle-stimulating hormone and testosterone remained stable. No meaningful changes in hematological, hepatic, or renal parameters, and adverse events low and comparable between groups.

Conclusions: Shatavari root extract for 56 days was safe and well-tolerated and resulted in clinically improvements in vasomotor symptoms, psychological well-being, sleep quality, and quality of life in peri- and postmenopausal women, supporting as a non-hormonal, holistic for management of menopausal symptoms.

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1. INTRODUCTION

Menopause is a natural biological transition characterized by the permanent cessation of menstruation and decline in ovarian function, typically occurring between 45 and 55 years of age. This transition is associated with a broad spectrum of vasomotor, psychological, somatic, and urogenital symptoms, including hot flushes, night sweats, sleep disturbances, mood changes, fatigue, and reduced quality of life [1-3]. Vasomotor symptoms, in particular, affect a substantial proportion of peri- and postmenopausal women and may persist for several years, significantly impairing daily functioning and overall well-being [4].

Hormone replacement therapy (HRT) remains the most effective intervention for alleviating menopausal vasomotor symptoms; however, its use is limited by safety concerns, contraindications, and patient reluctance, especially following reports linking long-term use to increased risks of breast cancer, thromboembolic events, and cardiovascular complications in certain populations [5-6]. Non-hormonal pharmacological options, including selective serotonin reuptake inhibitors and gabapentin, may offer partial relief but are often associated with adverse effects and limited efficacy across the multidimensional symptom profile of menopause [7]. Consequently, there is a growing demand for safe, well-tolerated, non-hormonal interventions that can address both physical and psychological aspects of menopausal health. Botanical and nutraceutical interventions have gained popularity among menopausal women due to their perceived safety and traditional use; however, many lack rigorous clinical validation through well-designed randomized controlled trials, limiting their acceptance in evidence-based clinical practice [8].

Several botanical interventions have been investigated for the management of menopausal symptoms including phytoestrogen-containing preparations such as soy isoflavones and red clover as well as non-estrogenic botanicals such as black cohosh. Phytoestrogenic substances are generally proposed to exert mild modulatory effects on estrogen receptor signaling, particularly through estrogen receptor-β pathways [9-10]. In contrast, black cohosh has been suggested to act primarily through central nervous system and serotonergic mechanisms rather than direct estrogen receptor activation [11]. Clinical studies of these interventions have reported variable benefits across symptom domains, reflecting differences in study design, population characteristics, and botanical composition [9, 12]. Consequently, there remains an ongoing interest in botanical strategies that integrate endocrine and neuroadaptive pathways to address the multidimensional nature of menopausal symptoms.

Adaptogenic botanicals are increasingly recognized for their ability to support hormonal balance through multisystem modulation, including regulation of the hypothalamic-pituitary-adrenal (HPA) axis, attenuation of stress responses, and stabilization of neuroendocrine signaling pathways [13]. By reducing cortisol dysregulation, improving sleep quality, and enhancing emotional resilience, such botanicals may help address menopausal symptoms beyond vasomotor complaints alone [14]. Botanicals that combine mild phytoestrogenic activity with adaptogenic properties [15] may therefore offer a more holistic therapeutic approach by addressing both endocrine and psychosomatic components of menopause. Shatavari (*Asparagus racemosus*) is traditionally classified as a *rasayana* and is reported to exhibit both estrogen-modulating and adaptogenic effects, providing a strong rationale for its evaluation in menopausal symptoms management [16].

The roots of Shatavari contain a diverse range of bioactive phytochemicals, including steroidal saponins (shatavarins I–IV), flavonoids, alkaloids, and polysaccharides, which have been reported to exhibit phytoestrogenic, adaptogenic, antioxidant, and immunomodulatory properties [17]. Preclinical studies suggest that Shatavari may modulate estrogen-responsive pathways, influence neuroendocrine and hypothalamic–pituitary–adrenal axis activity, and attenuate stress responses, although systematic clinical investigation in menopausal women remains limited [15]. However, despite its extensive traditional use, systematic clinical investigation of Shatavari for menopausal symptom management remains limited.

In this context, there is a clear need for robust clinical evidence to substantiate the role of Shatavari as a non-hormonal intervention for menopausal symptoms. This study was designed as a multicenter, randomized, double-blind, placebo-controlled, parallel-group clinical trial to evaluate the efficacy, safety, and tolerability of Shatavari root extract in the management of hot flashes and other climacteric symptoms in peri- and postmenopausal women.

2. MATERIALS AND METHODS

2.1. Ethical Considerations

This study was conducted in accordance with the International Council for Harmonisation (ICH) Guideline for Good Clinical Practice E6 (R3) , the New Drugs and Clinical Trials Rules 2019 (Government of India), the Indian Council of Medical Research (ICMR) National Ethical Guidelines for Biomedical and Health Research Involving Human Participants (2017), and the

Declaration of Helsinki (75th World Medical Association General Assembly, Helsinki, Finland, October 2024). The study protocol was reviewed and approved by duly constituted Ethics Committees (ECs) and was registered with the Clinical Trials Registry of India (CTRI) (Registration No.: CTRI/2025/05/086280). Written informed consent was obtained from all participants prior to the initiation of any study-related procedures. Eligibility screening was conducted only after informed consent had been provided. The informed consent documents were approved by the Ethics Committees and were presented in a language understandable to the participants. Participation was entirely voluntary, and no information provided during the consent process waived or appeared to waive any legal rights of the participants or relieved the investigator, institution, or sponsor of their responsibilities.

2.2. Study Design

This multicenter, randomized, double-blind, placebo-controlled, parallel-group clinical trial was conducted at two sites in Bengaluru, Karnataka, India: Santosh Hospital, Frazer Town, and Vagus Super Specialty Hospital Private Limited, Malleshwaram. The study was carried out between 13 May 2025 and 09 August 2025.this trial evaluated the effect of Shatavari root extract on menopausal symptoms in peri- and postmenopausal women over 56 days. Study visits were conducted at baseline and on Days 14, 28, 42, and 56. Screening and baseline procedures included collection of demographic characteristics, medical and medication history, and a comprehensive physical examination. Vital signs, including body temperature, pulse rate, respiratory rate, and systolic and diastolic blood pressure, were recorded. Baseline efficacy assessments included menopause-related symptom severity using the Menopause Rating Scale (MRS) [18,19] and menopause-specific quality of life using the MENQOL-I questionnaire [20]. Safety assessments included hematological, hepatic, renal, serological, hormonal, and routine urine investigations. Only participants who satisfied all prespecified inclusion and exclusion criteria on the basis of these evaluations were randomized into the study.

2.3. Participants

Eligible participants were sexually active women aged 45 to 55 years with menopausal symptoms, defined by MRS score of greater than or equal to 9-16 at screening. Both perimenopausal (amenorrhea >60 days within the preceding 12 months) and postmenopausal women (≥12 months of spontaneous amenorrhea) were included. Participants were required to report at least 10 hot flushes per week for at least 5 weeks and at least two additional menopausal symptoms, with a body mass index of 18-40 kg/m². Participants agreed to maintain their usual diet and physical activity, refrain from menopause-related medications or supplements, avoid caffeine and vigorous exercise prior to assessments, and provide written informed consent.

Women were excluded if they were pregnant, breastfeeding, planning pregnancy, or had undergone surgical menopause, had hypersensitivity to the study product, had clinically significant systemic disease, uncontrolled hypertension Participants using hormone therapy, psychotropic or centrally acting medications, or sleep medications, those with excessive caffeine intake, consumption of soy or estrogenic supplements, substance abuse, or prior exposure to an investigational product within three months were excluded. Individuals deemed unable or unwilling to comply with study procedures were also excluded.

2.4 Interventions

The current test item is a value added herbal extract, prepared with authenticated dried roots of (*Asparagus racemosus* Willd). Shatavari that were mechanically milled into a standardized coarse powder to ensure uniform solvent penetration. Extraction of the principal steroidal saponin, Shatavarin IV, with a limit of NLT 6% (by HPLC), was performed using a ethanol-based maceration technique, wherein the powdered roots were immersed in ethanol at ambient laboratory temperature (25 ± 2 °C) for 48 hour with continuous stirring to allow efficient extraction of bioactive constituents. Following maceration, the extract was filtered through a 5-µm cloth to remove particulate matter, and the filtrate was concentrated under reduced pressure at 50 °C to obtain a dried crude extract while minimizing thermal degradation. This enriched extract was subsequently blended with natural anti-oxidants to moderate the biological effects of Shatavarin-rich fractions, and also to make the final product content to NLT 5% Shatavarin IV by HPLC."

Test capsules and matching placebo capsules were supplied by India Glycols Ltd., Dehradun, India. Each test capsule contained 400 mg of Shatavari root extract with additives, while each placebo capsule is devoid of root extract. The test and placebo capsules were identical in appearance, including color, size, and shape, to maintain blinding. Bottles containing 30 capsules,

sufficient for a 28-day intervention period, were dispensed at the baseline visit and at Day 28. Participants were instructed to consume one capsule orally once daily with water after breakfast.

2.5 Primary, Secondary, and Exploratory Outcomes

The primary outcomes included assessment of hot flush severity and climacteric symptoms using the MRS questionnaire [18-19] and hot flush frequency using a hot flush diary [21], evaluated at baseline/screening and on Days 14, 28, 42, and 56.

Secondary outcomes included the assessment of perceived stress using the Perceived Stress Scale (PSS-10) [22], menopause-specific quality of life using the MENQOL-I [23], mood state using the Profile of Mood States (POMS-2) [24], sleep quality using the Sleep Quality Index [25], hormonal balance assessed by serum estradiol levels, and safety evaluated through laboratory investigations and adverse event monitoring. Stress and sleep quality were assessed at baseline, Day 28, and Day 56, while all other secondary outcomes were assessed at baseline/screening, and on Days 14, 28, 42, and 56. Exploratory outcomes included salivary cortisol levels and serum concentrations of follicle-stimulating hormone, luteinizing hormone, and testosterone. These were assessed at baseline, and on Days 14, 28, 42, and 56.

The primary endpoints were the change from baseline to Day 56 in MRS total and hot flush–related scores, as well as hot flush frequency as recorded in the hot flush diary. The secondary endpoints were the change from baseline to Day 56 in perceived stress, menopause-specific quality of life, mood, sleep quality, serum estradiol levels, and safety parameters. The exploratory endpoints were the change from baseline to Day 56 in salivary cortisol and serum follicle-stimulating hormone, luteinizing hormone, and testosterone levels.

2.6 Assessment Tools and Scoring

Menopause Rating Scale (MRS):

The Menopause Rating Scale (MRS) assesses 11 menopausal symptoms including hot flushes, heart discomfort, sleep problems, depressive mood, irritability, anxiety, physical and mental exhaustion, sexual problems, bladder problems, vaginal dryness, and joint and muscular discomfort. Each item is scored on a scale from 0 (no symptoms) to 4 (very severe symptoms). The total score is obtained by summing all item scores, with higher scores indicating greater symptom severity and poorer quality of life.

Menopause-Specific Quality of Life Questionnaire (MENQOL-I):

The MENQOL-I is a self-administered questionnaire comprising 32 items across four domains: vasomotor (3 items), psychosocial (7 items), physical (19 items), and sexual (3 items). Each symptom is first recorded as present or absent. If present, it is rated on a Likert scale from 0 (not bothersome) to 6 (extremely bothersome). Domain scores are calculated as the mean of items within each domain, with higher scores indicating greater impairment in quality of life.

Perceived Stress Scale (PSS-10):

The PSS-10 is a 10-item questionnaire used to measure perceived stress. Each item is scored on a scale of 0 to 4, resulting in a total score ranging from 0 to 40. Scores are interpreted as follows: 0–13 indicates low stress, 14–26 indicates moderate stress, and 27–40 indicates high perceived stress. Higher scores reflect greater levels of perceived stress.

Profile of Mood States (POMS-2):

The POMS-2 consists of 65 self-report items assessing seven mood domains: fatigue-inertia, anger-hostility, vigor-activity, confusion-bewilderment, depression-dejection, tension-anxiety, and friendliness. Each item is rated on a 5-point scale ranging from 0 ("not at all") to 4 ("extremely"). Scores for each domain are summed, with higher scores indicating greater mood disturbance, except for the vigor-activity and friendliness domains where higher scores indicate more positive mood states.

Pittsburgh Sleep Quality Index:

The Pittsburgh Sleep Quality Index (PSQI) is a widely used self-report instrument that assesses sleep quality and disturbances over a 1-month interval. It consists of 19 items generating seven component scores: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medication, and daytime dysfunction. Each component is scored on a scale from 0 (no difficulty) to 3 (severe difficulty). The component scores are summed to yield a global PSQI score

ranging from 0 to 21. A global score ≤5 indicates good sleep quality, whereas a score >5 reflects poor sleep quality. Higher scores denote greater impairment in sleep quality.

2.7 Sample Size

A meta-analysis evaluating the effect of dietary supplements on the management of climacteric symptoms in menopausal women reported a significantly greater reduction in hot flush frequency compared with placebo (pooled mean difference = 0.89; 95% CI, 0.26–1.52; $P < .005$) [26]. Based on these findings, a minimum clinically identifiable difference of 0.89 in the mean frequency of hot flushes between the test and placebo groups was assumed for the present study. Assuming a standard deviation of 1.4, 80% power, and a two-sided alpha of 0.05, 62 participants were required. To account for an anticipated dropout and non-compliance rate of approximately 15%, the sample size was increased to 70 participants, who were randomized equally to receive either the test product or a placebo (35 participants per group).

2.8 Randomization and Blinding

This study was conducted as a multicenter, randomized, double-blind, placebo-controlled, parallel-group clinical trial. Randomization numbers and corresponding interventions were assigned sequentially by the study statistician using a computer-generated randomization schedule prepared with SAS® software (version 9.4; PROC PLAN). All investigational product (IP) containers for both study interventions were pre-labeled with sequential container numbers and masked using a common batch number to ensure blinding. Following Ethics Committee approval, an unblinded pharmacist prepared the IPs by removing the original product labels and affixing blinded labels according to the randomization code. Access to the randomization code and the linkage between container numbers and study interventions was restricted exclusively to the unblinded pharmacist to maintain allocation concealment. After confirmation of participant eligibility at each study site, study personnel contacted the unblinded pharmacist to obtain the assigned randomization number and corresponding IP container number for dispensing. The assigned randomization number was recorded on the dispensed IP container. The randomization code was released to the data management team only after study completion for the purpose of statistical analysis. The principal investigator had conditional access to the blinded randomization code solely for participant safety considerations; however, no unblinding was required or occurred during the conduct of the study.

2.9 Statistical Methods

Participants with greater than or equal to 80% compliance to the study intervention were considered evaluable for efficacy and included in the statistical analyses. Descriptive summary statistics, including the number of participants, mean, standard deviation, minimum and maximum values, coefficient of variation (%), and standard error of the mean, were calculated for all continuous variables at each study visit. Baseline characteristics were summarized using means and standard deviations for continuous variables and counts and percentages for categorical variables. Between-group comparisons of continuous outcome variables were performed using a mixed-effects analysis of covariance (ANCOVA) model, with baseline values included as covariates to assess baseline-adjusted changes. The mixed-effects model accounted for within-subject variability and homogeneity of variances. Within-group changes from baseline were evaluated using paired t-tests. All statistical analyses were conducted using a two-sided significance level of 0.05, with $P < .05$ considered statistically significant. Statistical analyses were performed using SAS® software, version 9.4.

3. RESULTS AND DISCUSSION

3.1. Participant Flow

A total of 72 participants were screened, of whom 70 met the eligibility criteria and were enrolled in the study. All enrolled participants (N=70) were randomized and allocated equally to the test and placebo groups (35 participants per group) according to the randomization schedule. The per-protocol population comprised all 70 randomized participants, with 35 participants in each intervention group (Fig. 1).

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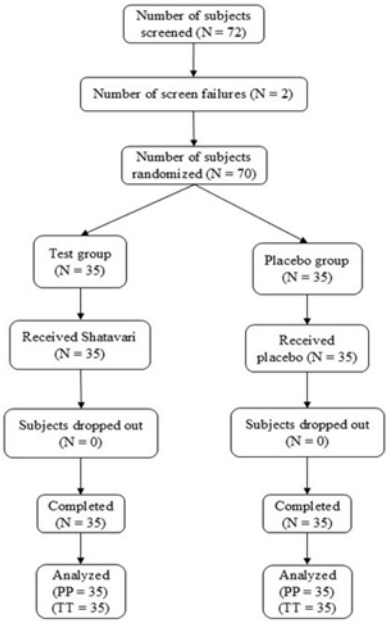

Figure 1. Participant Flow Diagram
ITT = Intent-to-treat; PP = per protocol

Fig. 1: Participant Flow Diagram

3.2. Baseline Demographic Characteristics

Baseline demographic characteristics were comparable between the test and placebo groups (Table 1). The mean age of participants was 50.00 ± 2.80 years in the test group and 50.10 ± 2.60 years in the placebo group. Mean body weight was 59.66 ± 8.24 kg in the test group and 61.51 ± 7.25 kg in the placebo group, mean height was 154.83 ± 9.34 cm and 156.94 ± 9.93 cm, mean body mass index (BMI) values were 24.96 ± 3.15 kg/m^2 for the test group and 25.10 ± 3.16 kg/m^2 for the placebo group respectively. No statistically significant differences between the two groups for any of the baseline demographic parameters, indicating that the groups were well balanced at baseline.

Table 1: Baseline Demographic Characteristics

Characteristics	Test	Placebo
Age (years)	50.00 ± 2.80	50.10 ± 2.60
Body weight (kg)	59.66 ± 8.24	61.51 ± 7.25
Height (cm)	154.83 ± 9.34	156.94 ± 9.93
BMI (kg/m^2)	24.96 ± 3.15	25.10 ± 3.16

Each values represents mean (SD) (n = 35). No statistically significant differences were found between the groups in any of the parameters

3.3. Primary Outcomes - Menopause Rating Scale and Hot Flush Frequency

At baseline, hot flush severity scores assessed using the MRS as well as the total and domain-specific scores were comparable between the test and placebo groups, indicating similar menopausal symptom severity at study entry. In the test group, hot flush severity decreased progressively over time, with a statistically significant reduction from baseline (2.40 ± 0.55) beginning from Day 28 (2.09 ± 0.37, $P = .0004$) onward, with further reductions at Day 42 (1.71 ± 0.52, $P < .0001$) and Day 56 (1.03 ±

0.17, $P < .0001$). In contrast, the placebo group showed no meaningful improvement, with scores remaining close to baseline throughout the study period (2.37 ± 0.65 at baseline vs. 2.43 ± 0.56 at Day 56).

Between-group differences favored the test group from Day 28 onward (P=.0018 at Day 28; P<.0001 at Days 42 and 56) (Table 2). In percentage terms, hot flush severity decreased by approximately 57% with the test product, whereas the placebo group showed a slight increase of about 2%, corresponding to an overall difference of about 59 percentage points.

Table 2: Effects of Shatavari on Hot Flush Severity Assessed using the Menopause Rating Scale (MRS)

Timeline	Test	t test value	P value	Placebo	t test value	P Value	ANCOVA value	Between-Group P-value‡
Baseline	2.40 ± 0.55	-	-	2.37 ± 0.65	-	-	-	-
Day 14	2.37 ± 0.55	1.00	0.3244	2.37 ± 0.65	-	-	0.95	0.3328
Day 28	2.09 ± 0.37	3.95	0.0004	2.31 ± 0.53	1.00	0.3244	10.57	0.0018
Day 42	1.7 ± 0.552	7.66	< .0001	2.34 ± 0.48	0.44	0.6613	50.86	< .0001
Day 56	1.03 ± 0.17	14.83	<0.0001	2.43 ± 0.56	-0.63	0.5349	260.94	< .0001

Each value represents mean (SD) (n = 35).

† Within-group changes from baseline were evaluated using paired t-tests (two-sided $\alpha = 0.05$).

‡ Between-group comparisons were performed using a mixed-effects ANCOVA model with baseline value as covariate and repeated measurements accounted for within subjects. LS mean differences and corresponding P-values are derived from the model.

Exact P-values are reported where available; values smaller than .0001 are shown as < .0001.

The total MRS score in the test group demonstrated a progressive and statistically significant reduction from baseline (13.3 ± 1.9), beginning at Day 14 (12.6 ± 1.7, $P < .0001$) and continuing through Day 56 (7.90 ± 1.3, $P < .0001$). In the placebo group, total MRS scores increased over time, from 13.5±1.8 at baseline to 15.5±3.0 at Day 56, with significant worsening at Day 14 (P=.0025), Day 28 (P=.0424), Day 42 (P=.0044), and Day 56 (P=.0005). Between-group comparisons showed that total MRS scores in the test group were significantly lower than placebo from Day 14 onward ($P = .0012$), ; P<.0001 at Days 28, 42, and 56) Table 3 (). In percentage terms, the test product showed ~41% reduction, whereas the placebo was associated with an approximately 15% increase, giving a net advantage of about 56 percentage points.

Table 3: Effects of Shatavari on Total Menopause Rating Scale (MRS) Score

Timeline	Test	t test value	P value	Placebo	t test value	P Value	ANCOVA value	Between-Group P-value‡
Baseline	13.30 ± 1.90	-	-	13.50 ± 1.80	-	-	-	-
Day 14	12.60 ± 1.70	6.8	<0.0001	13.20 ± 1.80	3.26	0.0025	11.53	0.0012
Day 28	11.40 ± 1.70	8.81	<0.0001	14.00 ± 2.10	-2.11	0.0424	63.81	<0.0001
Day 42	10.50 ± 1.90	10.96	<0.0001	14.30 ± 2.10	-3.06	0.0044	106.35	<0.0001
Day 56	7.90 ± 1.30	15.88	<0.0001	15.50 ± 3.00	-3.84	0.0005	186.68	<0.0001

Each value represents mean (SD) (n = 35).

† Within-group changes from baseline were evaluated using paired t-tests (two-sided $\alpha = 0.05$).

‡ Between-group comparisons were performed using a mixed-effects ANCOVA model with baseline value as covariate and repeated measurements accounted for within subjects. LS mean differences and corresponding P-values are derived from the model.

Exact P-values are reported where available; values smaller than .0001 are shown as < .0001.

Analysis of MRS domains revealed consistent improvements in the test group. Psychological domain scores decreased significantly from baseline (6.0 ± 1.4) starting at Day 14 (5.8 ± 1.3, $P = .0032$) and were significantly lower than placebo at Days 28 (5.1 ± 1.3, $P < .0001$), 42 (4.9 ± 1.4, $P < .0001$), and 56 (3.7 ± 1.1, $P < .0001$) (Table 4). This corresponded to an approximately 38% reduction with the test product versus an approximately 14% increase with placebo, a difference of about 52 percentage points.

Table 4: Effects of Shatavari on Psychological Domain Score of the Menopause Rating Scale (MRS)

Timeline	Test	t test value	P value	Placebo	t test value	P Value	ANCOVA value	Between-Group P-value‡
Baseline	6.00 ± 1.40	-	-	5.70 ± 1.30	-	-	-	-
Day 14	5.80 ± 1.30	3.17	0.0032	5.60 ± 1.30	1.79	0.0831	1.90	0.1727
Day 28	5.10 ± 1.30	6.34	<0.0001	6.00 ± 1.60	-2.03	0.0500	29.91	<0.0001
Day 42	4.90 ± 1.40	6.73	<0.0001	6.20 ± 1.50	-3.02	0.0048	43.93	<0.0001
Day 56	3.70 ± 1.10	9.50	<0.0001	6.50 ± 1.70	-3.38	0.0018	95.32	<0.0001

Each value represents mean (SD) (n = 35).

† Within-group changes from baseline were evaluated using paired t-tests (two-sided $\alpha = 0.05$).

‡ Between-group comparisons were performed using a mixed-effects ANCOVA model with baseline value as covariate and repeated measurements accounted for within subjects. LS mean differences and corresponding P-values are derived from the model.

Exact P-values are reported where available; values smaller than .0001 are shown as < .0001.

Somatic domain scores of test group showed significant reductions from Day 14 onward (4.8 ± 1.3, $P < .01$ to 4.4 ± 1.1, $P < .0001$ at Day 28, 3.9 ± 1.1, $P < .0001$ at Day 42 and 2.9 ± 0.8, $P < .0001$ at Day 56) and were significantly lower than placebo from Day 14 ($P = .0007$) through Day 56 ($P< .0001$)

(Table 5). In percentage terms, the test product showed ~43% reduction, whereas the placebo group showed an increase of ~9% over the same period, yielding ~52 percentage-point between-group difference.

Table 5: Effects of Shatavari on Somatic Domain Score of the Menopause Rating Scale (MRS)

Timeline	Test	t test value	P value	Placebo	t test value	P Value	ANCOVA value	Between-Group P-value‡
Baseline	5.10 ± 1.60	-	-	5.40 ± 1.30	-	-	-	-
Day 14	4.80 ± 1.30	3.26	0.0025	5.30 ± 1.30	1.0	0.3244	12.58	0.0007
Day 28	4.40 ± 1.10	4.51	<0.0001	5.50 ± 1.60	-0.77	0.4466	31.14	<0.0001
Day 42	3.90 ± 1.10	7.26	<0.0001	5.60 ± 1.50	-1.56	0.1284	68.80	<0.0001
Day 56	2.90 ± 0.80	10.34	<0.0001	5.90 ± 1.70	-2.65	0.0121	140.38	<0.0001

Each value represents mean (SD) (n = 35).

† Within-group changes from baseline were evaluated using paired t-tests (two-sided α = 0.05).

‡ Between-group comparisons were performed using a mixed-effects ANCOVA model with baseline value as covariate and repeated measurements accounted for within subjects. LS mean differences and corresponding P-values are derived from the model.

Exact P-values are reported where available; values smaller than .0001 are shown as < .0001.

Urogenital domain scores also improved significantly from baseline (2.2 ± 1.2) in the test group beginning at Day 14 (2.0 ± 1.0, *P* = .0173), with greater reductions compared with placebo observed from Day 28 (1.8 ± 0.90, *P* = .0005) to Day 42 (1.7 ± 0.7, *P* = .0002) and Day 56 (1.4 ± 0.8, *P* < .0001) (Table 6). In percentage terms, the test product showed ~36% reduction, whereas the placebo group showed an increase of ~20% over56 days, corresponding to a ~ 56 percentage-point greater improvement with the test product.

Table 6: Effects of Shatavari on Urogenital Domain Score of the Menopause Rating Scale (MRS)

Timeline	Test	t test value	P value	Placebo	t test value	P Value	ANCOVA value	Between-Group P-value‡
Baseline	2.20 ± 1.20	-	-	2.50 ± 1.70	-	-	-	-
Day 14	2.00 ± 1.00	2.50	0.0173	2.30 ± 1.70	2.24	0.0318	0.47	0.4946
Day 28	1.80 ± 0.90	3.43	0.0016	2.60 ± 1.80	-0.90	0.3733	13.22	0.0005
Day 42	1.70 ± 0.70	3.68	0.0008	2.50 ± 1.80	-0.30	0.7678	15.14	0.0002
Day 56	1.40 ± 0.80	4.96	<0.0001	3.00 ± 1.60	-3.63	0.0009	56.89	<0.0001

Each value represents mean (SD) (n = 35).

† Within-group changes from baseline were evaluated using paired t-tests (two-sided α = 0.05).

‡ Between-group comparisons were performed using a mixed-effects ANCOVA model with baseline value as covariate and repeated measurements accounted for within subjects. LS mean differences and corresponding P-values are derived from the model.

Exact P-values are reported where available; values smaller than .0001 are shown as < .0001.

Assessment of hot flush frequency using participant diaries demonstrated a significant reduction compared to placebo by Day 28 (1.45 ± 0.21, *P* < .01), with further reductions at Days 42 (1.19 ± 0.19, *P* < .0001) and 56 (0.80 ± 0.15, *P* < .0001) (Table 7). In percentage terms, the test product showed an approximate 51% reduction from Day 14 to Day 56, whereas the placebo group showed only an approximately 2% reduction, representing an approximate 49-percentage-point greater reduction with the test product.

Table 7: Effects of Shatavari on Hot Flush frequency

Timeline	Test	Placebo	ANCOVA value	Between-Group P-value‡
Average from baseline to Day 14	1.64 ± 0.22	1.64 ± 0.27	-0.07	0.9456
Average from Day 14 to Day 28	1.45 ± 0.21	1.62 ± 0.21	-3.45	0.0010
Average from Day 28 to Day 42	1.19 ± 0.19	1.63 ± 0.21	-9.17	<0.0001
Average from Day 42 to Day 56	0.80 ± 0.15	1.60 ± 0.29	-14.52	<0.0001

Each value represents mean (SD) (n = 35).

‡ Between-group comparisons were performed using a mixed-effects ANCOVA model with baseline value as covariate and repeated measurements accounted for within subjects. LS mean differences and corresponding P-values are derived from the model.

Exact P-values are reported where available; values smaller than .0001 are shown as < .0001.

Overall, supplementation resulted in statistically significant and clinically meaningful improvements in hot flush severity, frequency, and total and domain-specific MRS symptom scores compared with placebo over the 56-day intervention period.

3.4 Secondary Outcomes

3.4.1. Perceived Stress Scale (PSS-10) Results

Baseline PSS-10 scores were comparable between the test and placebo groups, indicating similar levels of perceived stress at study entry (Table 8). In the test group, PSS-10 scores decreased significantly at Day 28 (17.3 ± 2.4, $P < .0001$) and showed a further reduction at Day 56 (13.8 ± 2.2, $P < .0001$). The placebo group showed no significant change, with mean scores remaining close to baseline at both post-baseline visits. The reductions with the test product were significantly greater than those with placebo at Day 28 (P=.0002) and Day 56 (P<.0001). These findings indicate a significant and sustained reduction in perceived stress over the 56-day intervention period.

Table 8: Effects of Shatavari on Perceived Stress Scale (PSS-10) Scores

Timeline	Test	Placebo	ANCOVA value	p-value (Test Vs Placebo) Baseline adjusted
Baseline	19.5 ± 3.1	18.5 ± 3.4		Not Applicable
Day 28	17.3 ± 2.4****###	18.5 ± 3.8	16.00	0.0002*
Day 56	13.8 ± 2.2****####	19.0 ± 3.8	84.59	<.0001*

Each value represents mean (SD) (n = 35). ****P< .0001 compared to respective baseline within a group; ###P< .001; ####P< .0001 - compared to the placebo.

‡ Between-group comparisons were performed using a mixed-effects ANCOVA model with baseline value as covariate and repeated measurements accounted for within subjects. LS mean differences and corresponding P-values are derived from the model.

Exact P-values are reported where available; values smaller than .0001 are shown as < .0001.

3.4.2. Menopause-Specific Quality of Life (MENQOL-I) Results

Baseline MENQOL-I total and domain scores were comparable between the test and placebo groups (Table 3), indicating similar menopause-related quality-of-life impairment at study entry. In the test group, the MENQOL-I total score showed a progressive and statistically significant reduction from baseline beginning at Day 14 ($P < .0001$), with further improvements observed at Days 28 ($P = .0003$), 42 ($P < .0001$), and 56 ($P < .0001$). In contrast, the placebo group showed no improvement, with total MENQOL-I scores remaining stable or worsening over time. Domain-wise analysis demonstrated consistent benefits of the test product. The vasomotor domain score in the test group showed a significant reduction from baseline starting at Day 28 ($P < .0001$), with further marked reductions at Days 42 ($P < .0001$) and 56 ($P < .0001$). The placebo group exhibited no meaningful improvement in vasomotor domain scores across the study period. Psychosocial domain scores in the test group declined significantly from Day 14 ($P < .05$), with greater reductions at Day 28 ($P = .0005$), Day 42 ($P < .0001$), and Day 56 ($P < .0001$); these reductions were also significantly greater than placebo from Day 14 onward, while placebo scores increased progressively. Similarly, the physical domain score demonstrated a significant and time-dependent reduction in the test group from Day 14 onward (P< .001 to P< .0001), with significantly lower scores compared with placebo at Days 28, 42, and 56. The placebo group showed no improvement and a trend towards worsening physical domain scores. For the sexual domain, scores in the test group showed a gradual numerical reduction over time, reaching statistical significance from baseline

(*P* = .0019) and compared with placebo at Day 56 (*P* < .0001). The placebo group demonstrated a significant increase in sexual domain scores by Day 56, indicating worsening of symptoms (Table 9). Overall, the test product produced meaningful improvements in menopause-specific quality of life across total and domain scores over 56 days.

Table 9: Effects of Shatavari on Menopause-Specific Quality of Life (MENQOL-I) Scores

MENQOL-I Items	**Timeline**	**Test**	t test value	P value	Placebo	t test value	P Value	ANCOVA Value	Between-Group P-value‡
Total score	Baseline	2.78 ± 0.38			2.70 ± 0.44				
	Day 14	2.73 ± 0.35	4.92	< .0001	2.69 ± 0.43	1.04	0.3062	5.66	0.0202
	Day 28	2.63 ± 0.27	4.00	0.0003	2.81 ± 0.48	-3.10	0.0039	25.52	< .0001
	Day 42	2.49 ± 0.27	6.35	< .0001	2.83 ± 0.5	-2.91	0.0064	44.55	< .0001
	Day 56	2.19 ± 0.21	11.48	<0.0001	2.95 ± 0.51	-3.77	0.0006	117.57	< .0001
Vasomotor domain score	Baseline	4.44 ± 1.00			4.21 ± 1.15				
	Day 14	4.41 ± 1.00	1.35	0.1884	4.25 ± 1.12	-1.00	0.3244	1.90	0.1732
	Day 28	4.07 ± 1.01	4.43	< 0.0001	4.31 ± 1.03	-1.36	0.1827	17.34	< .0001
	Day 42	3.48 ± 0.91	6.30	< 0.0001	4.26 ± 1.07	-0.47	0.6421	32.15	< .0001
	Day 56	2.70 ± 0.48	12.08	< 0.0001	4.31 ± 1.02	-0.64	0.5248	125.33	< .0001
Psychosocial domain score	Baseline	3.14 ± 0.87			2.82 ± 0.72				
	Day 14	3.07 ± 0.83	2.70	0.0108	2.83 ± 0.71	-0.62	0.5386	4.39	0.0399
	Day 28	2.88 ± 0.65	3.85	0.0005	3.00 ± 0.73	-2.56	0.0151	16.90	0.0001
	Day 42	2.73 ± 0.61	4.66	< 0.0001	3.05 ± 0.70	-2.69	0.0111	25.28	< .0001
	Day 56	2.38 ± 0.49	7.23	< 0.0001	3.14 ± 0.79	-2.90	0.0064	54.66	< .0001
Physical domain score	Baseline	2.41 ± 0.36			2.44 ± 0.45				
	Day 14	2.38 ± 0.32	4.07	0.0003	2.42 ± 0.45	1.89	0.0666	3.45	0.0677
	Day 28	2.34 ± 0.29	2.39	0.0223	2.55 ± 0.48	-2.77	0.0089	15.33	0.0002
	Day 42	2.27 ± 0.28	3.80	0.0006	2.57 ± 0.49	-2.57	0.0149	22.49	< .0001
	Day 56	2.05 ± 0.26	8.35	< 0.0001	2.68 ± 0.5	-3.91	0.0004	78.64	< .0001
Sexual domain score	Baseline	2.52 ± 1.00			2.55 ± 1.33				
	Day 14	2.49 ± 1.01	0.82	0.4198	2.51 ± 1.29	1.71	0.0965	0.02	0.8750
	Day 28	2.41 ± 0.82	1.18	0.2468	2.50 ± 1.23	0.74	0.4614	0.33	0.5679
	Day 42	2.32 ± 0.76	1.65	0.1085	2.51 ± 1.21	0.58	0.5660	1.58	0.2137
	Day 56	2.12 ± 0.75	3.36	0.0019	2.86 ± 1.26	-2.47	0.0188	22.26	< .0001

Each value represents mean (SD) (n = 35).

† Within-group changes from baseline were evaluated using paired t-tests (two-sided α = 0.05).

‡ Between-group comparisons were performed using a mixed-effects ANCOVA model with baseline value as covariate and repeated measurements accounted for within subjects. LS mean differences and corresponding *P*-values are derived from the model.

Exact *P*-values are reported where available; values smaller than .0001 are shown as < .0001.

3.4.3. Profile of Mood States (POMS-2)

Baseline POMS-2 total mood disturbance and domain scores were comparable between the test and placebo groups, indicating similar mood profiles at study entry (Table 4). In the test group, the Total Mood Disturbance (TMD) score showed reduction from baseline beginning at Day 14 ($P < .0001$), with further reductions observed at Days 28, 42, and 56 ($P < .0001$ at all-time points). In contrast, the placebo group demonstrated no improvement, with TMD scores increasing over time, indicating worsening mood disturbance. The improvements observed with test substance were also significantly greater than placebo from Day 14 onward ($P = .0035$ at Day 14 and $P < .0001$ at subsequent visits).

Analysis of negative mood domains showed consistent improvements in the test group. Anger-Hostility scores decreased significantly from baseline by Day 56 ($P = .0036$) and were significantly lower than placebo at Days 42 and 56 ($P = .0034$ and $P < .0001$, respectively). Confusion-Bewilderment decreased significantly from Day 28 onward ($P < .0001$) and was lower than placebo at Day 28 and all subsequent visits ($P < .0001$. Depression–Dejection scores decreased significantly from baseline starting at Day 14 ($P = .0031$), with further reductions at Days 28 ($P = .0014$), 42 ($P < .0001$) and 56 ($P < .0001$), and were significantly lower in comparison to placebo at Days 28 ($P = .0077$), 42 ($P < .0001$), and 56 ($P < .0001$). Fatigue-Inertia scores also demonstrated a significant and time-dependent reduction in the test group from Day 14 onward ($P = .0336$), with scores consistently lower than placebo at Days 28 ($P = .0110$), 42 ($P = .0005$), and 56 ($P < .0001$). Tension-Anxiety also decreased significantly from Day 14 ($P = .0049$) and remained significantly lower than placebo from Day 14 onward ($P = .0355$ to $P < .0001$). In contrast, the placebo group showed no consistent improvement across negative mood domains, with several domains worsening over time (Table 10).

Positive mood domains demonstrated opposite trends. In the test group, Vigor-Activity scores increased significantly from baseline beginning at Day 14 ($P < .0001$) and continued to rise through Day 56 ($P < .0001$), with scores statistically significant in comparison to placebo at all post-baseline visits ($P = .0465$ to $P < .0001$). Friendliness scores also showed statistical significant increase from baseline in the test group starting at Day 14 ($P = .0008$), with progressively greater improvements observed through Day 56 ($P < .0001$), and were significantly higher than placebo from Day 28 ($P < .0001$) onward. The placebo group showed no meaningful change in positive mood domains. Overall, supplementation resulted in sustained improvements across total mood disturbance, negative mood states, and positive mood dimensions compared with placebo.

Table 10: Effects of Shatavari on Profile of Mood States (POMS-2) Scores.

POMS-2 Items	Timeline	Test group	t test value	P value	Placebo group	t test Value	P value	ANCOVA Value	Between-Group P -value‡
Total Mood Disturbance	Baseline	61.1 ± 22.8			58.2 ± 21.9				
	Day 14	58.3 ± 21.2	5.43	< 0.0001	57.9 ± 21.5	0.56	0.5808	9.19	0.0035
	Day 28	49.7 ± 17.4	5.12	< 0.0001	60.9 ± 20.2	-2.16	0.0376	37.97	< .0001
	Day 42	41.9 ± 14.5	6.42	< 0.0001	62.8 ± 21.	-2.70	0.0108	65.20	< .0001
	Day 56	26.9 ± 13.6	8.78	< 0.0001	64.8 ± 21.3	-2.29	0.0284	111.63	< .0001
Anger- hostility	Baseline	11.4 ± 5.4			11.6 ± 5.7				

POMS-2 Items	Timeline	Test group	t test value	P value	Placebo group	t test Value	P value	ANCOVA Value	Between-Group P -value‡
	Day 14	11.1 ± 5.3	2.09	0.0437	11.7 ± 5.5	-0.16	0.8722	1.73	0.1926
	Day 28	10.9 ± 3.6	0.73	0.4682	12.0 ± 5.4	-1.05	0.3031	2.25	0.1380
	Day 42	10.0 ± 3.6	1.66	0.1055	12.6 ± 5.5	-1.86	0.0716	9.25	0.0034
	Day 56	8.4 ± 2.5	3.13	0.0036	13.5 ± 5.4	-2.75	0.0096	33.85	< .0001
POMS-(Confusion-Bewilderment)	Baseline	18.1 ± 5.1			17.3 ± 4.7				
	Day 14	17.9 ± 4.8	1.97	0.0576	17.1 ± 4.4	1.18	0.2449	0.07	0.7924
	Day 28	16.3 ± 4.0	4.88	< 0.0001	17.9 ± 4.2	-2.05	0.0484	31.30	< .0001
	Day 42	14.7 ± 3.6	5.77	< 0.0001	18.0 ± 4.1	-1.99	0.0543	46.45	< .0001
	Day 56	12.1 ± 3.7	7.19	< 0.0001	18.0 ± 4.0	-1.44	0.1603	68.03	< .0001
POMS-(Depression-Dejection)	Baseline	17.8 ± 6.9			17 ± 7.3				
	Day 14	17.5 ± 6.7	3.19	0.0031	17 ± 6.9	-0.05	0.9607	0.31	0.5786
	Day 28	15.7 ± 5.3	3.48	0.0014	17.5 ± 6.7	-0.60	0.5507	7.54	0.0077
	Day 42	13.9 ± 4.3	5.05	< 0.0001	17.3 ± 6.6	-0.41	0.6857	20.60	< .0001
	Day 56	11.4 ± 3.1	6.16	< 0.0001	17.3 ± 6.6	-0.40	0.6902	43.98	< .0001
POMS-(Fatigue-Inertia)	Baseline	10.1 ± 4.1			8.8 ± 4.1				
	Day 14	9.6 ± 3.5	2.21	0.0336	8.9 ± 4.1	-0.77	0.4466	3.61	0.0617
	Day 28	8.8 ± 2.8	2.69	0.0110	9.8 ± 3.7	-2.89	0.0066	14.74	0.0003
	Day 42	8.2 ± 2.6	3.85	0.0005	9.9 ± 3.7	-2.66	0.0119	23.64	< .0001
	Day 56	6.3 ± 1.4	5.42	< 0.0001	10.4 ± 3.7	-3.17	0.0032	59.81	< .0001
POMS-(Tension-Anxiety)	Baseline	14.7 ± 4.8			14.8 ± 4.2				
	Day 14	14.2 ± 4.2	3.01	0.0049	14.9 ± 4.1	-0.12	0.9034	4.60	= .0355
	Day 28	12.5 ± 4.2	5.43	< 0.0001	15.0 ± 3.9	-0.64	0.5254	27.85	< .0001
	Day 42	11.6 ± 4.2	5.42	< 0.0001	15.9 ± 4.2	-2.32	0.0267	39.76	< .0001

POMS-2 Items	Timeline	Test group	t test value	P value	Placebo group	t test Value	P value	ANCOVA Value	Between-Group P -value‡
	Day 56	8.5 ± 2.6	7.79	< 0.0001	16.6 ± 3.9	-2.76	0.0092	127.11	< .0001
POMS-(Vigor-Activity)	Baseline	11.1 ± 4.6			11.3 ± 4.5				
	Day 14	12.0 ± 4.9	-4.43	< 0.0001	11.6 ± 4.6	-1.79	0.0831	4.12	0.0465
	Day 28	14.3 ± 4.2	-6.09	< 0.0001	11.3 ± 3.7	0.08	0.9378	32.74	< .0001
	Day 42	16.4 ± 3.3	-8.19	< 0.0001	11.0 ± 3.7	0.69	0.4967	88.59	< .0001
	Day 56	19.7 ± 5.4	-11.87	< 0.0001	11.1 ± 3.6	0.27	0.7882	99.70	< .0001
POMS-(Friendliness)	Baseline	8.4 ± 3.5			8.5 ± 3.3				
	Day 14	8.8 ± 3.7	-3.67	0.0008	8.7 ± 3.5	-0.90	0.3733	0.14	0.7118
	Day 28	10.4 ± 2.9	-5.63	< 0.0001	8.7 ± 3.2	-0.53	0.5973	17.56	< .0001
	Day 42	11.7 ± 2.6	-6.48	< 0.0001	8.8 ± 3.3	-0.76	0.4522	26.68	< .0001
	Day 56	14.2 ± 3.8	-9.71	< 0.0001	8.2 ± 2.9	0.53	0.6012	77.44ss	< .0001

Each value represents mean (SD) (n = 35).

† Within-group changes from baseline were evaluated using paired t-tests (two-sided $\alpha = 0.05$).

‡ Between-group comparisons were performed using a mixed-effects ANCOVA model with baseline value as covariate and repeated measurements accounted for within subjects. LS mean differences and corresponding *P*-values are derived from the model.

Exact *P*-values are reported where available; values smaller than .0001 are shown as <.0001.

3.4.4. Sleep Quality

Baseline Sleep Quality Index global scores were comparable between the test and placebo groups, indicating similar sleep quality at study entry (Table 11). In the test group, the global sleep quality score showed a statistically significant improvement from baseline at Day 28 ($p = .0006$), with a further significant improvement observed at Day 56 ($P < .0001$). These improvements were also statistically significant in comparison to placebo group at both post-baseline time points ($P < .0001$). In contrast, the placebo group showed no improvement in sleep quality, with a statistically significant worsening by Day 56 compared with baseline ($P = .0332$) By Day 56, the between-group difference was pronounced in favor of the test product, indicating a sustained improvement in sleep quality over the 56-day intervention period.

Table 11: Effects of Shatavari on Sleep Quality Index Global Scores

Timeline	Test	t test value	P value	Placebo	t test value	P value	ANCOVA value	Between-Group P-value‡
Baseline	7.1 ± 2.8			6.8 ± 2.7				
Day 28	6.1 ± 2.1	3.77	0.0006	7.1 ± 2.5	-1.62	0.1151	20.30	< .0001
Day 56	5.1 ± 1.8	5.75	< 0.0001	7.5 ± 2.9	-2.22	0.0332	41.15	< .0001

Each value represents mean ± SD (n = 35).

† Within-group changes from baseline were evaluated using paired t-tests (two-sided α = 0.05).

‡ Between-group comparisons were performed using a mixed-effects ANCOVA model with baseline value as covariate and repeated measurements accounted for within subjects. LS mean differences and corresponding *P*-values are derived from the model.

Exact *P*-values are reported where available; values smaller than .0001 are shown as < .0001

3.4.5. Effect of Shatavari on Hormone Levels

Baseline serum estradiol, salivary cortisol, follicle-stimulating hormone (FSH), luteinizing hormone (LH), and total testosterone levels were comparable between the test and placebo groups (Table 12). In the test group, serum estradiol levels showed a gradual and statistically significant increase from baseline, with significant within-group improvements observed from Day 28 (*P* = .0364) onward (*P* = .0364 at Day 42 and *P* = .0329 at Day 56). Estradiol levels in the test group were also statistically increased in comparison to placebo at all post-baseline visits (*P* = .0273 at Day 14, *P* = .0029 at Day 28, *P* = .0021 at Day 42, and *P* = .0007 at Day 56). In contrast, the placebo group exhibited a statically significant reduction in estradiol levels from baseline, indicating a divergent hormonal trend between the groups (Table 12). In percentage terms, the test product showed an approximate 7% increase from baseline, whereas the placebo group showed a decrease of ~14% from baseline over 56 days, representing an approximate 21 percentage-point greater increase with the test product. No statistically significant within-group change in salivary cortisol was observed in the test group; however, salivary cortisol levels were significantly lower compared with placebo at Days 42 (*P* = .0352) and 56 (*P* = .0063). In contrast, the placebo group showed a statistically significant increase in salivary cortisol from baseline at multiple post-baseline visits, suggesting a relative worsening of stress-related hormonal response (Table 12).

Table 12: Changes in Hormonal Parameters from Baseline to Day 56

Hormone Levels	Timeline	Test	t test value	P value	Placebo	t test value	P Value	ANCOVA value	Between-Group P-value‡
Serum estradiol (pg/mL)	Baseline	27.38 ± 7.70			30.08 ± 11.71				
	Day 14	27.99 ± 6.91	-0.93	0.3597	26.45 ± 8.10	2.30	0.0275	5.09	0.0273
	Day 28	28.79 ± 7.45	-2.18	0.0364	26.15 ± 8.09	2.53	0.0164	9.57	0.0029
	Day 42	28.89 ± 7.71	-2.22	0.0329	26.01 ± 7.95	2.60	0.0138	10.28	0.0021
	Day 56	29.25 ± 7.31	-2.91	0.0063	25.91 ± 7.80	2.61	0.0135	12.78	0.0007
Salivary cortisol (ng/mL)	Baseline	23.18 ± 5.28			21.89 ± 4.83				
	Day 14	23.28 ± 4.0	-0.14	0.8871	23.23 ± 4.64	-2.63	0.0128	0.99	= .3236
	Day 28	22.84 ± 3.99	0.47	0.6428	23.41 ± 3.83	-2.53	0.0163	2.80	= .0991
	Day 42	22.47 ± 4.21	0.99	0.3302	23.32 ± 4.42	-2.72	0.0101	4.62	= .0352
	Day 56	22.11 ± 4.02	1.46	0.1539	23.50 ± 4.47	-3.03	0.0047	7.95	= .0063
Follicle - Stimulating Hormone assessmen	Baseline	87.79 ± 16.32			82.86 ± 21.00				
	Day 14	85.50 ± 10.61	1.00	0.3251	85.44 ± 14.55	-0.91	0.3697	0.59	= .4456
	Day 28	84.90 ± 10.86	1.18	0.2451	85.27 ± 14.25	-0.84	0.4086	0.75	= .3892

t (µIU/mL)	Day 42	84.72 ± 10.97	1.26	0.2172	84.81 ± 13.80	-0.67	0.5053	0.56	= .4561
	Day 56	84.62 ± 10.92	1.31	0.1979	84.61 ± 14.24	-0.61	0.5435	0.54	= .4630
Luteinizing Hormone assessment (µIU/mL)	Baseline	48.11 ± 14.75			48.20 ± 13.98				
	Day 14	45.01 ± 10.96	2.14	0.0392	50.09 ± 10.29	-0.96	0.3416	7.69	= .0072
	Day 28	44.39 ± 11.00	2.50	0.0174	50.16 ± 10.17	-1.00	0.3249	9.81	= .0026
	Day 42	43.96 ± 11.07	2.73	0.0099	49.07 ± 10.02	-0.44	0.6619	7.52	= .0078
	Day 56	43.80 ± 10.63	2.90	0.0064	49.53 ± 10.48	-0.68	0.5013	9.78	= .0026
Testosterone-total assessment (ng/mL)	Baseline	0.38 ± 0.13			0.39 ± 0.14				
	Day 14	0.37 ± 0.13	1.72	0.0954	0.39 ± 0.13	1.28	0.2108	0.92	= .3408
	Day 28	0.38 ± 0.13	0.96	0.3460	0.38 ± 0.14	1.33	0.1914	0.02	= .8805
	Day 42	0.36 ± 0.12	1.71	0.0961	0.38 ± 0.14	1.52	0.1374	0.18	= .6722
	Day 56	0.37 ± 0.14	1.36	0.1825	0.39 ± 0.14	-0.16	0.8707	1.40	= .2404

Each value represents mean ± SD (n = 35).

† Within-group changes from baseline were evaluated using paired t-tests (two-sided α = 0.05).

‡ Between-group comparisons were performed using a mixed-effects ANCOVA model with baseline value as covariate and repeated measurements accounted for within subjects. LS mean differences and corresponding Z-values are derived from the model.

Exact *P*-values are reported where available; values smaller than .0001 are shown as <.0001.

FSH levels remained stable over the study period in both groups, with no statistically significant within-group or between-group differences observed at any time point, indicating no effect of the intervention on FSH concentrations (Table 12). In the test group, LH levels showed a statistically significant reduction from baseline beginning at Day 14 ($P = 0.0392$), with sustained reductions through Day 56 ($P = .0064$). These reductions were statistically significant when compared to placebo at all post-baseline visits (.0072 at Day 14, $P = .0026$ at Day 28, $P = .0078$ at Day 42, and $P = .0026$ at Day 56). In contrast, LH levels in the placebo group remained unchanged or showed a slight numerical increase over time (Table 12). In percentage terms, the test product produced an approximate 9% reduction in LH, whereas placebo showed an approximate 3% increase over 56 days, representing an approximate 12-percentage-point difference. Total testosterone levels remained unchanged throughout the study in both the test and placebo groups, with no statistically significant within-group or between-group differences observed, indicating hormonal safety with respect to androgen levels (Table 12).

Overall, the test product was associated with favorable modulation of estradiol, cortisol, and LH levels, while maintaining stability of FSH and testosterone concentrations, supporting both efficacy-related endocrine effects and hormonal safety.

SAFETY

A small number of adverse events were reported in both the test and placebo groups during the study (Table 13). In the test group, gastritis was reported by four subjects, compared with two subjects in the placebo group. Hyperthermia (fever) was reported by two subjects in the test group and one subject in the placebo group. Common cold was reported by two subjects in the test group, with no cases reported in the placebo group. All adverse events were mild in intensity, self-limiting, and

resolved without the need for discontinuation of the investigational product or additional medical intervention. No serious adverse events were reported, and there were no clinically significant differences in the incidence or nature of adverse events between the groups. . Overall, the investigational product was well-tolerated over the study duration.

Table 13: Summary of Adverse Events

Adverse events	Test (n=7)	Placebo (n=3)
Gastritis	4	2
Hyperthermia (Fever)	2	1
Cold	2	0

Each value represents the number of subjects.

Safety was assessed through a comprehensive evaluation of hematological parameters, liver function tests, and renal function tests at baseline and after 56 days of intervention. All measured parameters remained within normal physiological ranges throughout the study period in both groups (Table 14). Hematological indices, including hemoglobin, total and differential leukocyte counts, platelet count, and red blood cell indices, remained stable with no evidence of hematological toxicity. Liver function parameters, including bilirubin fractions, serum proteins, and hepatic enzymes (AST, ALT, ALP, and GGT), showed no clinically meaningful elevations, indicating the absence of hepatotoxicity. Renal function markers, including blood urea, serum creatinine, and blood urea nitrogen, also remained within normal limits, with no signs of renal impairment (Table 14).

Table 14 Laboratory Safety Evaluation Results

Safety Parameters	Baseline		Day 56		Reference range
	Test	Placebo	Test	Placebo	
Hematology					
Hemoglobin (gm/dl)	12.28 ± 1.58	12.23 ± 1.55	12.61 ± 0.88	12.42 ± 0.96	12 – 17 g/dL
Total WBC (cells/µl)	9205.71 ± 4278.81	8725.71 ± 3341.92	8262.86 ± 1406.93	8017.14 ± 994.24	4,000 – 11,000 cells/µL
Neutrophils (%)	66.66 ± 10.41	63.37 ± 9.72	61.03 ± 7.12	62.37 ± 6.23	40 – 70 %
Lymphocytes (%)	27.43 ± 10.32	30.77 ± 8.76	33.37 ± 6.96	31.91 ± 6.17	20 – 40 %
Eosinophils (%)	2.11 ± 0.93	2.14 ± 0.69	2.20 ± 0.41	2.11 ± 0.32	1 – 6 %
Monocytes (%)	3.80 ± 1.41	3.71 ± 1.36	3.40 ± 0.69	3.60 ± 0.74	2 – 10 %
Basophils (%)	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0 – 1 %
Platelet count (lakh cells/µl)	2.85 ± 0.70	2.96 ± 0.68	2.79 ± 0.50	2.90 ± 0.45	1.5 – 4.0 lakh cells/µL
RBC (million cells/µl)	4.18 ± 0.91	4.06 ± 0.57	4.17 ± 0.30	4.13 ± 0.35	4.0 – 5.5 million cells/µL
PCV (%)	37.14 ± 4.84	36.71 ± 4.72	37.76 ± 2.66	37.25 ± 2.87	36 – 50 %
MCV (fL)	82.35 ± 11.73	82.91 ± 11.42	85.46 ± 6.11	85.80 ± 5.56	80 – 100 fL

Safety Parameters	Baseline		Day 56		Reference range
	Test	Placebo	Test	Placebo	
MCH (pg)	28.10 ± 2.68	28.40 ± 2.55	28.89 ± 2.36	29.35 ± 2.49	26–32 pg0 – 20 mm/hr
MCHC (%)	32.87 ± 1.22	32.54 ± 1.51	33.15 ± 1.18	33.49 ± 0.90	32 – 36 %
ESR (mm/hr)	19.49 ± 10.25	21.54 ± 15.64	18.91 ± 4.90	19.46 ± 6.95	0 – 20 mm/hr
Liver function tests					
Total Bilirubin (mg/dL)	1.00 ± 0.36	0.94 ± 0.42	0.75 ± 0.15	0.77 ± 0.17	0.3 – 1.2 mg/dL
Direct Bilirubin (mg/dL)	0.34 ± 0.21	0.30 ± 0.19	0.19 ± 0.04	0.19 ± 0.06	0.0 – 0.3 mg/dL
Indirect Bilirubin (mg/dL)	0.67 ± 0.20	0.64 ± 0.26	0.56 ± 0.12	0.58 ± 0.12	0.2 – 0.9 mg/dL
Total Protein (g/dL)	6.29 ± 0.37	6.33 ± 0.46	6.50 ± 0.31	6.42 ± 0.35	6.0 – 8.3 g/dL
Serum albumin (g/dL)	3.73 ± 0.30	3.72 ± 0.45	4.06 ± 0.12	4.03 ± 0.12	3.5 – 5.0 g/dL
Serum globulin (g/dL)	2.56 ± 0.40	2.61 ± 0.38	2.44 ± 0.35	2.39 ± 0.31	2.0 – 3.5 g/dL
A/G Ratio	1.52 ± 0.33	1.47 ± 0.29	1.71 ± 0.31	1.72 ± 0.25	1.0 – 2.2
SGOT (U/L)	25.83 ± 7.85	26.63 ± 9.52	22.97 ± 4.26	22.77 ± 4.45	5 – 40 U/L
SGPT (U/L)	26.80 ± 8.36	26.77 ± 10.61	24.43 ± 3.74	24.34 ± 5.16	5 – 45 U/L
ALP (U/L)	85.03 ± 20.76	88.37 ± 30.37	86.51 ± 9.06	85.34 ± 10.95	44 – 147 U/L
GGT (U/L)	18.58 ± 3.94	17.89 ± 4.80	16.46 ± 2.40	16.41 ± 3.20	5 – 60 U/L
Renal function Tests					
Blood urea (mg/dL)	27.06 ± 5.84	27.40 ± 5.36	25.80 ± 3.55	25.89 ± 2.49	15 – 40 mg/dL
Serum creatinine (mg/dL)	0.87 ± 0.12	0.88 ± 0.14	0.92 ± 0.06	0.93 ± 0.07	0.6 – 1.3 mg/dL
Blood urea nitrogen (mg/dL)	12.63 ± 2.72	12.90 ± 2.55	12.04 ± 1.66	11.98 ± 1.21	7 – 20 mg/dL

Each value represents the mean (SD) (n=35). No significant difference observed in any of the parameters within the group and between the groups. A/G , Albumin/Globulin; ALP, Alkaline phosphatase; ESR , Erythrocyte sedimentation rate; GGT , gamma-glutamyl transferase; MCH , Mean corpuscula hemoglobin; MCHC , Mean corpuscula hemoglobin concentration; MCV, Mean corpuscular volume; PCV, Packed cell volume; RBC, Red blood cells; SGOT , serum glutamic oxaloacetic transaminase; SGPT , serum glutamic pyruvic transaminase; WBC, White blood cells.

No statistical test was done for laboratory evaluation

Overall, no clinically meaningful or test item-related adverse changes were observed in hematological, hepatic, or renal safety parameters over the 56-day intervention period.

3.5 Discussion

This multicenter, randomized, double-blind, placebo-controlled clinical study demonstrated that supplementation with current Shatavari (*Asparagus racemosus*) root extract for 56 days resulted in significant improvements in vasomotor symptoms, menopausal symptom severity, perceived stress, mood, sleep quality, menopause-specific quality of life, and selective hormonal parameters, while maintaining a favorable safety profile in peri- and postmenopausal women.

Vasomotor symptoms such as hot flushes are primarily linked to estrogen withdrawal and altered hypothalamic thermoregulation during menopause [27]. In the present study, Shatavari supplementation produced a progressive reduction in hot flush severity and frequency from Day 14 onwards, along with improvements in total and somatic scores from Day 14, and psychological and urogenital scores from Day 28 onwards. Similar improvements in menopausal symptoms have been reported with other Shatavari preparations [27-28], although the timing and magnitude of improvement varied across studies in total MRS (only at Week 8) somatic (only at Week 8), and urogenital (only at Week 8) scores [27, 29] with no significant improvements in hot flush [27] or significant improvements in hot flush observed only at Day 60 [28] compared to placebo. Shatavari roots are rich in steroidal saponins (shatavarins I–IV), which have been shown to exhibit estrogen-like activity in preclinical models without causing overt hormonal stimulation [16, 15]. The gradual and sustained symptom improvement observed in this study supports a modulatory rather than replacement mechanism, differentiating Shatavari from conventional hormone therapy. Differences in onset of improvement across studies may reflect variations in extract standardization, dosage, baseline symptom severity, and study design. Other herbal preparations namely *Rheum Rhaponticum* root extract 400 mg per day [21] and Fenugreek extract at 500 mg per day [30] have been reported to reduce menopausal symptoms but with longer treatment period of more than 8 weeks.

Menopause associates with increased stress, anxiety, and mood disturbances, mediated in part by dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis [31-32]. In this study, Shatavari supplementation significantly reduced perceived stress and improved multiple POMS-2 mood domains, including reductions in anxiety, depression, fatigue, and anger, alongside increases in vigor and friendliness. These findings are in agreement with preclinical studies demonstrating adaptogenic, anxiolytic, and antidepressant-like effects of *Asparagus racemosus*, potentially mediated through cortisol modulation, antioxidant activity, and neurotransmitter regulation [33-35]. However, other Shatavari preparation in a clinical study has not shown any effect in PSS and POMS [27]. Although salivary cortisol did not show a statistically significant within-group reduction, the significant between-group differences observed at later time points are consistent with a stress-buffering effect, supporting the psychological outcomes.

Sleep disturbances are a prominent complaint during the menopausal transition and are closely linked to vasomotor symptoms and psychological stress [1]. In the present study, Shatavari supplementation led to significant improvements in sleep quality, while placebo-treated participants experienced worsening sleep scores. The sleep improvements observed in this study may result from multiple complementary mechanisms. Preclinical evidence demonstrates that Shatavari's GABAergic and serotonergic effects reduce anxiety-related hyperarousal without producing sedation [33], thereby addressing a primary driver of insomnia in menopausal women and additionally, through the reduction of vasomotor symptoms (hot flushes, night sweats). Similar improvements in sleep quality have been reported in a study with 500 mg dose of *Asparagus racemosus* root extract standardized to 5% total shatavarins, where Regensburg Insomnia Scale was used for sleep assessments [28].

Improvements in MENQOL-I total and domain scores here indicate a meaningful enhancement in overall menopause-related quality of life. This comprehensive domain improvement distinguishes the current intervention from most comparable shorter-duration trials in the literature. While a 24-week randomized trial [36] demonstrated a 20.8% improvement in MENQOL-I scores with *Asparagus racemosus* 500 mg compared to minimal placebo change ($P < .0001$), earlier 8-week investigations reported comparatively smaller magnitude improvements, suggesting a potential duration-dependent effect. In contrast, the test substance evaluated in the present study demonstrated clinically meaningful improvements within 8 weeks. A perimenopausal study [37] reported only marginal total MENQOL-I significance ($P = .043$) with no statistically significant individual domain improvements at a dose of 300 mg daily, while a multicenter 8-week trial [27] found numerical but statistically non-significant

MENQOL-I improvements with *Asparagus racemosus* ($P = .117$). The present study's demonstration of significant improvements across all MENQOL-I domains at 56 days suggests either superior extract standardization and bioavailability, population-specific responsiveness characteristics, or optimized dosing relative to prior 8-week interventions. These findings suggest that Shatavari supplementation is associated not only with reductions in acute menopausal symptom burden but also with improvements in subject-perceived quality of life and functional well-being, outcomes that are central to subject-centered menopause management. The consistent improvements across vasomotor, psychosocial, physical, and sexual domains observed in this study suggest a holistic benefit, aligning with Shatavari's traditional classification as a *rasayana* (rejuvenative tonic) [15].

Shatavari supplementation was associated with a gradual but significant increase in serum estradiol levels (~21%) that remained within physiological limits, along with a significant reduction in luteinizing hormone (~12%), without significant changes in follicle-stimulating hormone or testosterone. During and after menopause, LH levels rise markedly as ovarian estrogen and progesterone production decline and negative feedback on the hypothalamic–pituitary axis is lost [38]. Sustained elevation of LH is a characteristic endocrine feature of the postmenopausal state and has been implicated alongside estrogen withdrawal, in cognitive changes and in the altered neuroendocrine milieu associated with vasomotor cognitive symptoms [39].

In this context, the modest increase in estradiol observed in the present study may have partially restored hypothalamic-pituitary feedback regulation, thereby contributing to the observed attenuation of LH levels and stabilization of FSH. Notably, clinical studies with other Shatavari preparations have reported variable hormonal responses, including no significant increase in estradiol [28-29], delayed estradiol elevation after 120 days [40], and reductions in FSH compared to placebo [29,40],suggesting possible formulation- or duration-dependent effects.

Overall, this hormonal profile aligns with earlier experimental findings indicating that Shatavari may enhance estrogenic tone or receptor responsiveness rather than act as a direct estrogen replacement [28, 41]. Importantly, the maintenance of estradiol within physiological range and the stability of testosterone and FSH levels suggest endocrine modulation without evidence of hormonal overstimulation, consistent with prior safety observations [37].

The favorable safety profile observed in this study is consistent with earlier clinical and toxicological evaluations of Shatavari, which report good tolerability and absence of clinically relevant adverse effects at commonly used doses [27-29, 37, 42]. The absence of adverse effects on hematological, hepatic, and renal parameters further supports its suitability for use in menopausal women.

The clinical relevance of the 400 mg daily dose used in this study warrants consideration. Prior investigations have evaluated lower doses, including 50 mg and 100 mg preparations, with variable statistical outcomes and effect sizes [40]. In comparison, the present study demonstrated statistically significant improvements across multiple endpoints at 400 mg, consistent with a possible dose-response relationship. Importantly, studies utilizing higher shatavarin-standardized extracts (e.g., approximately 15%) have reported effect sizes within a similar range indicating that both total dose and phytochemical standardization may influence clinical outcomes. However, differences in study design, duration, baseline severity, and extract composition preclude direct cross-study equivalence. Controlled dose-ranging trials would be required to establish definitive dose-response relationships.

Taken together, the multi-domain improvements observed in this study contribute to the evolving clinical and experimental literature on *Asparagus racemosus* and are broadly aligned with its longstanding traditional use in women's reproductive and menopausal health [42-43]. While variability across studies highlights the influence of formulation, dosage, and population characteristics, the present findings add further evidence supporting its role as a botanical option in menopause management.

The strengths of this study include its randomized, double-blind, placebo-controlled, multicenter design, comprehensive assessment of both efficacy and safety outcomes, and use of validated instruments across multiple domains of menopausal health. Notably, statistically significant improvements were observed despite inclusion of participants with mild-to-moderate baseline symptom severity, whereas some earlier studies have preferentially enrolled women with more severe menopausal symptoms. Limitations include the moderate sample size, short intervention duration, and lack of long-term follow-up, which restrict conclusions regarding sustained efficacy and long-term safety. Future studies should explore longer intervention periods and broader populations to further define clinical applicability.

4. CONCLUSION

Taken together, the findings of this study contribute to the growing clinical evidence that Shatavari root extract may provide multi-domain benefits in peri- and postmenopausal women, including improvements in vasomotor symptoms, psychological well-being, sleep quality, and quality of life, with favorable modulation of selective hormonal parameters and a reassuring safety profile. These results position Shatavari as a potential non-hormonal botanical option for the management of menopausal symptoms.

DECLARATIONS

Ethics approval and consent to participate

The study protocol was approved by the Santosh Hospital Institutional Ethics Committee, Approval No. SHIEC/EC_APP/APR-2025/05. The study protocol was approved by Ethics Committees (ECs) and was registered with the Clinical Trials Registry of India (CTRI) (Registration No.: CTRI/2025/05/086280). Written informed consent was obtained from all participants prior to the initiation of any study-related procedures. Eligibility screening was conducted only after informed consent had been provided.

Consent for publication

Not Applicable.

Availability of data and materials

The original contributions presented in this study are included in this article. Further inquiries can be directed to the corresponding author(s).

Competing interests

The authors declare that they have no competing interests related to this work. The sponsor participated in study design and manuscript preparation but did not influence the interpretation of the results or the decision to publish.

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AUTHORS' CONTRIBUTIONS

P.K.B.: Conceptualization, Methodology, Project administration. R.K.Y.: Methodology, Formal analysis, Data curation, Writing-review & editing. H.T.M.: Investigation, Writing-original draft, Validation, Writing-review & editing. P.N.: Data curation, Writing-review & editing. M.S.K.: Conceptualization, Methodology, Project administration. N.S.S.C.: Methodology, Formal analysis, Data curation, Writing-review & editing. J.D.: Data curation, Supervision. A.P.: Data curation, Writing-review & editing, Project administration.

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