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Sage (Salvia officinalis) consumption and its association with prolactin levels among women:
"An exploratory community-based study"

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ABSTRACT

Women's health plays a pivotal role in community well-being and public health. Hormonal imbalances, particularly those involving prolactin, can significantly impact reproductive health, leading to menstrual irregularities, galactorrhea, infertility, and other complications. Salvia officinalis (sage) is a medicinal herb traditionally used for its therapeutic properties, including its potential to regulate hormonal balance and alleviate symptoms associated with reproductive disorders. Despite its widespread use, clinical evidence regarding its effects on prolactin levels remains limited. This study aimed to investigate the impact of Salvia officinalis on serum prolactin levels and associated clinical symptoms in women. Single-arm pre–post interventional pilot study was conducted with 50 women aged 15–52 years residing in Traghan, Libya. Participants consumed sage tea two to three times daily for two weeks, following standardized preparation guidelines. Blood samples were collected before and after the intervention to

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assess prolactin levels using the i-Chroma device. Paired t-tests were applied to determine the statistical significance of changes in prolactin levels. Additionally, participants were monitored for changes in common symptoms related to hyperprolactinemia, including chest pain, menstrual irregularities, and galactorrhea. The results demonstrated a statistically significant reduction in prolactin levels following the intervention (P = 0.001). The mean prolactin levels decreased notably after two weeks of sage consumption, indicating a consistent treatment effect. A significant reduction in serum prolactin levels was observed after the two-week intervention with Salvia officinalis. Moreover, participants reported substantial alleviation of clinical symptoms, including a reduction in chest pain, normalization of menstrual cycles, and decreased occurrences of galactorrhea. No severe adverse effects were reported, highlighting the safety of short-term sage use. In conclusion, Salvia officinalis was associated with a reduction in prolactin levels and improvement in related reproductive symptoms within the study population. However, given the exploratory design of the study and the absence of a control group, causal relationships cannot be established. Therefore, these findings should be interpreted with caution and considered hypothesis-generating. Further well-designed randomized controlled trials with larger sample sizes and longer follow-up periods are required to confirm these results before any clinical recommendations can be made.

Keywords: Salvia officinalis; Prolactin; Hyperprolactinemia; Hormonal balance; Women’s health; Reproductive health.

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استهلاك الميرمية [Salvia officinalis) وعلاقته بمستويات البرولاكتين لدى النساء : دراسة استكشافية مجتمعية

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الملخص:

تلعب صحة المرأة دورًا محوريًا في رفاه المجتمع والصحة العامة. يمكن أن تؤثر الاختلالات الهرمونية، خصوصًا تلك التي تتعلق بالبرولاكتين، بشكل كبير في الصحة الإنجابية، مما يؤدي إلى عدم انتظام الدورة الشهرية، وثرّ اللبن، والعقم، ومضاعفات أخرى. تُعدّ *Salvia officinalis* (الميرمية) عشبة طبية استُخدمت تقليديًا لخصائصها العلاجية، بما في ذلك قدرتها المحتملة على تنظيم التوازن الهرموني وتخفيف الأعراض المرتبطة باضطرابات الجهاز التناسلي. وعلى الرغم من استخدامها الواسع، لا تزال الأدلة السريرية المتعلقة بتأثيرها على مستويات البرولاكتين محدودة. هدفت هذه الدراسة إلى تقصّي تأثير العشبة الميرمية على مستويات البرولاكتين في مصل الدم والأعراض السريرية المصاحبة لدى النساء.

أُجريت دراسة استطلاعية تدخلية أحادية الذراع قبل–بعد على 50 امرأة تتراوح أعمارهن بين 15 و52 سنة من المقيمات في تراغن، ليبيا. استهلكت المشاركات شاي الميرمية مرتين إلى ثلاث مرات يوميًا لمدة أسبوعين، باتباع إرشادات تحضير موحّدة. جُمعت عينات الدم قبل وبعد التدخل لتقييم مستويات البرولاكتين باستخدام جهاز i–Chroma. طُبّق اختبار (t) للعينات المزدوجة لتحديد الدلالة الإحصائية للتغيرات في مستويات البرولاكتين. بالإضافة إلى ذلك، تمت متابعة المشاركات لرصد التغيرات في الأعراض الشائعة المرتبطة بفرط برولاكتين الدم، بما في ذلك ألم الصدر، وعدم

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انتظام الدورة الشهرية، وثرّ اللبن.

أظهرت النتائج انخفاضًا ذا دلالة إحصائية في مستويات البرولاكتين بعد التدخل (P = 0.001). أنخفض متوسط مستويات البرولاكتين بشكل ملحوظ بعد أسبوعين من استهلاك الميرمية، مما يشير إلى تأثير علاجي متسق. لوحِظ انخفاضٌ ملحوظ في مستويات هرمون البرولاكتين في مصل الدم بعد التدخل باستخدام نبات الميرمية لمدة أسبوعين. علاوة على ذلك، أفادت المشاركات بانخفاض ملحوظ في الأعراض السريرية، بما في ذلك تراجع ألم الصدر، وانتظام الدورة الشهرية، وانخفاض حالات ثرّ اللبن. لم تُسجَّل أي آثار جانبية شديدة، مما يبرز سلامة الاستخدام قصير المدى للميرمية.

في الختام، ارتبط استخدام العشبة الميرمية بانخفاض في مستويات البرولاكتين وتحسّن في الأعراض الإنجابية المصاحبة ضمن عينة الدراسة. ومع ذلك، ونظرًا للطبيعة الاستكشافية للدراسة وغياب مجموعة ضابطة، لا يمكن إثبات وجود علاقة سببية. لذلك ينبغي تفسير هذه النتائج بحذر واعتبارها توليدية للفرضيات. وتظل الحاجة قائمة إلى إجراء دراسات عشوائية محكَّمة ذات تصميم أقوى، وبعينات أكبر وفترات متابعة أطول، للتحقق من هذه النتائج قبل تقديم أي توصيات سريرية.

الكلمات المفتاحية :الميرمية؛ البرولاكتين؛ فرط برولاكتين الدم؛ التوازن الهرموني؛ صحة المرأة؛ الصحة الإنجابية.

INTRODUCTION

Women’s health is strongly associated with overall community well-being and socioeconomic stability. Evidence from local community studies highlights the importance of health awareness initiatives in promoting safe and informed therapeutic practices [1]. Hormonal imbalances and high prolactin levels may interfere with functions considered as community health of women. Salvia officinalis, or sage, is a medicinal herb which has been used for a long time regarding therapeutic applications related to hormonal balance. Some experimental studies suggest a potential effect of Salvia officinalis on prolactin (PRL) regulation, which is one of the key hormones associated with lactation. However, increased levels of prolactin cause hyperprolactinemia, which in turn are related to various health issues, such as irregular

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menstrual cycles, infertility, and galactorrhea [2].

Hormones are biochemical messengers secreted by endocrine glands in small quantities and transported through the bloodstream to target organs, where they regulate various physiological functions. Prolactin plays an essential role in lactation, but when increased or decreased from normal levels, it can affect the reproductive health of a woman in the form of abnormalities in her menstrual cycle and difficulty conceiving [3]. Increased prolactin levels are frequently due to pituitary tumor or other dysfunctions of the endocrine system [4]. Potential to modulate prolactin levels from sage plants may, thus, provide natural remedies to these hormonal imbalances [2,5]. Recent studies suggest that Salvia officinalis contains phytoestrogenic compounds that are similar to estrogen and have an effect on prolactin secretion, binding to the estrogen receptor and thus decreasing prolactin levels [2]. Salvia officinalis, on the other hand, is said to act by way of dopaminergic pathways, where there occurs inhibition of prolactin release by dopamine, thus controlling prolactin levels [5]. This dual mechanism may contribute to the potential role of sage in regulating prolactin levels [6,7].

The findings of studies on Salvia officinalis extracts as used in animal models showed great reductions in prolactin levels but without disturbing other hormones such as estrogen, progesterone, or testosterone [5]. Such characteristic targeted action on prolactin is arguably a promising facet for sage's clinical application in treating hyperprolactinemia [9]. A similar finding was reported by Li et al., who undertook a 30-day hormonal assessment of rats treated with plant extracts, including sage, and where prolactin levels were found to have declined markedly with time [8]. Their findings also implied improvement in some reproductive health markers, further reemphasizing the significance of sage in hormonal pathways regulation [2].

Rich has been attributed to the antioxidant character of Salvia officinalis, which also renders it renown for alleviating oxidative stress-a condition, mostly blamed for systemic hormonal dysregulation [5]. It may lead to several conditions with hormonal imbalances, and sage's other effects may even add to the effectiveness of this plant as a natural remedy by reducing

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oxidative stress [3,10]. Besides prolactin, Salvia officinalis has also been shown to have some effect on other major hormones responsible for reproduction. Continuous application of sage treatment in animal subjects resulted in stabilized levels of progesterone and testosterone [3]. Such effects imply that sage may be beneficial in providing a holistic approach to managing hormonal imbalances present with diseases such as polycystic ovary syndrome (PCOS) and menopause [9,11]. Furthermore, it has been documented that the estrogenic actions of sage could be useful in menstrual cycle regulation and fertility improvement [6,12].

In postmenopausal women, Salvia officinalis has alleviated symptoms such as hot flashes, night sweats, and mood swings. Randomized controlled trials indicated that sage brought remarkable improvements in sexual health and overall well-being, thus demonstrating its broad impact on hormonal regulation in this population [7]. Its clinical potential extends beyond prolactin regulation and may serve as an alternative remedy for some menopausal symptoms [9]. Moreover, the findings emphasize the critical role of early detection in enhancing patient response to treatment and achieving optimal therapeutic outcomes [14]. Moreover, various researchers have evaluated the use of sage in the treatment of hormonal imbalances. Aromatherapy with sage eases menopausal symptoms such as hormonal imbalance [10]. Oral sage extract also helped reduce hot flashes and night sweats that are generally associated with hormonal fluctuations during menopause [12]. Sage also improved sexual function with hormonal stability in postmenopausal women [11].

These findings indicated the effect of sage on health outcomes beyond reproductive health [4]. Although these results seem promising, it will still require more studies to be performed about standardizing sage extracts and proving the ethical and long-term safety and efficacy of itself in regulating the prolactin levels. Some authors would further emphasize the need for mechanistic studies to conclude how plant-derived components such as sage affect the cellular processes of DNA replication and transcription as well [9]. These insights might further shed light on sage's promise in the management of hormonal imbalance and

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improvement in clinical outcomes [3]. Therefore, the purpose of this pilot study is to investigate the effect of Salvia officinalis on prolactin levels among women with hyperprolactinemia and to explore its potential role in improving hormonal balance within a community health care context. This exploratory investigation aims to assess the potential effectiveness of sage as a natural, accessible, and complementary intervention that may contribute to enhancing women's reproductive health and overall well-being.

MATERIALS AND METHODS

Study design, setting and study period

This study was designed as a single-arm pre-post interventional pilot study conducted among women with elevated serum prolactin levels in Traghan, Libya. Between July 18 and August 23, 2022.

Sample size and sampling technique

Women attending Traghan Hospital and selected private outpatient clinics were screened for serum prolactin levels. Women with elevated prolactin levels who agreed to participate were enrolled in the study. A total of 50 women, including married and unmarried participants aged between 15 and 52 years, were included.

Inclusion and exclusion criteria

Inclusion criteria were women aged 15–52 years with elevated serum prolactin levels who agreed to participate in the study.

Exclusion criteria included pregnancy, lactation, known pituitary disorders, thyroid disease, chronic renal disease, and the use of medications known to affect prolactin levels.

Data collection and assessment of clinical symptoms

Participants were asked to complete a questionnaire that was distributed in collaboration with gynecologists at Traghan Hospital and selected private outpatient clinics. Clinical symptoms, including menstrual irregularities, galactorrhea [milk discharge from the breast), breast pain, and depressive symptoms, were assessed at baseline and after the two-week intervention using a structured questionnaire completed by the participants in collaboration with the attending gynecologists. Symptoms were recorded as present or absent for each participant.

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Intervention and follow-up

The patients were instructed to consume *Salvia officinalis* (sage) for two weeks. The dosage consisted of drinking one cup of water containing a small amount of dried sage leaves [non-ground) two to three times daily according to the physician's recommendation.

After the two-week intervention period, blood samples were reanalyzed to assess changes in serum prolactin levels.

Devices*:*

i-CHROMA™ analyzer: This device was used to measure serum prolactin levels using an immunoassay method according to the manufacturer's instructions.

Reference range: The normal reference range for serum prolactin in women was considered to be 3–25 ng/m.

Preparation of sage infusion*:*

Dried sage leaves (Salvia officinalis) were used in their whole, non-ground form. An appropriate amount of dried leaves [approximately 2–3 g, equivalent to 5–7 whole dried leaves) was added to 250 mL of freshly boiled water (heat turned off after boiling). The mixture was covered and allowed to steep for 20 minutes, then filtered and consumed warm or cold according to participant preference.

Dosage regime*:*

Participants consumed one cup per dose, either twice or three times daily, depending on individual tolerance and adherence, resulting in an estimated total daily intake of 4–9 g of dried sage leaves.

Statistical analysis

Data were analyzed using the Statistical Package for the Social Sciences (SPSS). Descriptive statistics were used to summarize the study variables. Continuous variables were expressed as mean ± standard deviation. The paired t-test was used to compare serum prolactin levels before and after the consumption of Salvia officinalis. The Chi-square test was applied to examine the relationship between categorical variables, such as marital status and treatment response. A p-value of less than 0.05 was considered statistically significant.

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ETHICS

Prior to collecting samples and conducting analyses, informed consent was obtained from all participants in the study. The study's objectives were explained to the participants, ensuring they understood all procedures involved and provided voluntary consent to participate. Confidentiality of medical information and personal data was guaranteed in accordance with ethical standards for medical research.

RESULTS

The table (1) mean value of the studied parameter demonstrated a noticeable reduction following the intervention. Before treatment, the mean value was approximately 48, whereas it decreased to about 37 after treatment. The mean difference between the two measurements was 11.23 units, indicating a substantial decline after the intervention. The 95% confidence interval (CI) for the mean difference ranged from 6.63 to 15.82, which does not include zero, suggesting that the observed change is statistically significant. Furthermore, the error bars show minimal overlap between the pre- and post-treatment measurements, supporting the consistency and reliability of the observed reduction. Overall, these findings indicate that the intervention was associated with a significant decrease in the measured outcome, reflecting a clear treatment-related effect.

Table (1): Paired T for Before Treatment - After Treatment

	N	Mean	St-Dev	-T Value	Value -P
Before Treatment	50	47.99	24.67		
After Treatment	50	36.76	20.49	4.91	0.001
Difference	50	11.23	16.18		
95% (CI for mean difference: 15.82;6.63)					
With Normal Distribution					

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Table (2) presents the distribution of participants according to age group and marital status. The largest proportion of participants was observed in the 25–34 age group, accounting for 40% of the total sample, with an equal number of married and single women (n = 10 each). This was followed by the 15–24 age group, which represented 34% of the participants, where single women (n = 13) outnumbered married women (n = 4). Participants aged 35– 43 constituted 20% of the sample, with a slightly higher number of single women (n = 6) compared to married women (n = 4). The smallest proportion of participants was found in the 44–52 age group (6%), consisting exclusively of married women (n = 2). Overall, the distribution indicates a higher representation of younger women, particularly single women, in the study sample.

Table (2): Distribution of study participants according to age group and marital status

Age group	Number of Single Women	Number of Married Women	Total of Percentage
15 -24	13	4	34%
25 -34	10	10	40%
35 - 43	6	4	20%
44 - 52	1	2	6%

Table (3) demonstrates a marked reduction in the prevalence of all reported symptoms after taking the medication. Chest pain decreased from 30% before treatment to 10% after treatment, while irregular menstrual cycles declined from 52% to 15%. Milk discharge from the breast was reduced from 10% to 2%, and depressive symptoms were completely absent after treatment, decreasing from 6% to 0%. These findings indicate an overall improvement in symptoms following medication use.

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Table (3): Comparison of Symptoms Before and After Taking the Medication

Symptoms	Before Treatment (%)	(reatmentT fterA%)
Chest pain	30%	10%
Irregular Menstrual Cycle	52%	15%
Milk Discharge from Breast	10%	2%
Depression	6%	0%

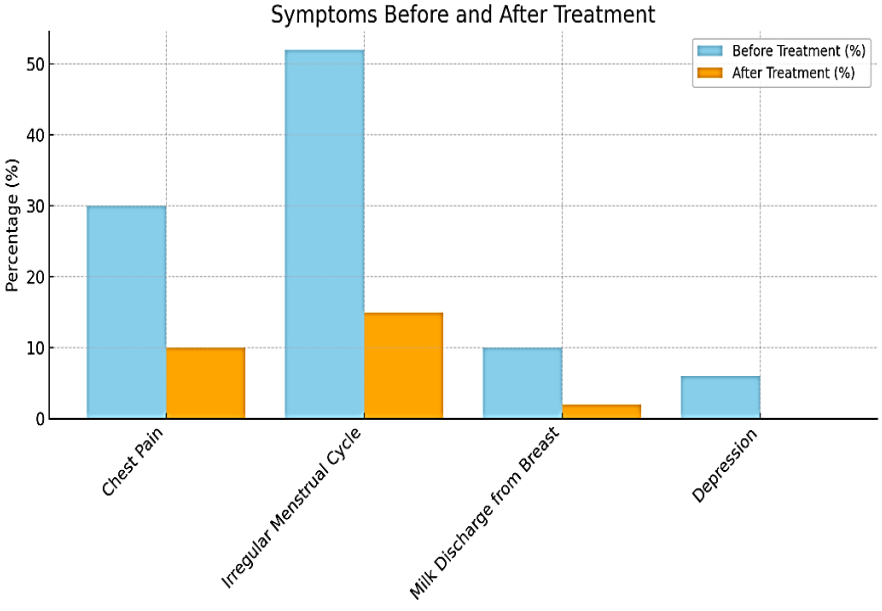

Figure 1. illustrates the previous and post-treatment stages in terms of percentages.

DISCUSSION

The present study aimed to evaluate the effect of the applied therapeutic intervention on several clinical and functional parameters, with particular emphasis on quantitative changes in the studied variable as well as improvements in associated clinical symptoms. The findings demonstrated a clear and statistically

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significant improvement following the treatment period, reflecting the effectiveness of the intervention and highlighting its potential role in regulating disorders associated with hormonal and neuroendocrine alterations.

The results presented in Table (1) revealed a statistically significant reduction in the mean value of the studied parameter following treatment. The mean value decreased from approximately 48 before intervention to about 37 after treatment, with a mean difference of 11.23 units. The 95% confidence interval (6.63–15.82) did not include zero, confirming that this reduction was statistically significant and unlikely to have occurred by chance. Moreover, the minimal overlap observed between the error bars before and after treatment indicates consistency in the response among participants and supports the reliability of the observed therapeutic effect.

This reduction can be attributed to the biological and pharmacological properties of the therapeutic agents used, particularly plant-derived extracts, which have been reported to possess anti-inflammatory, antioxidant, and neuromodulator effects [15,16]. These properties are especially relevant in conditions characterized by hormonal imbalance accompanied by both psychological and physical symptoms, such as hyperprolactinemia and premenstrual-related disorders [17].

Furthermore, previous studies have demonstrated that phenolic compounds, including rosmarinic acid and carnosic acid, as well as flavonoids and diterpenes, play a significant role in inhibiting inflammatory processes and reducing oxidative stress. Such mechanisms may positively influence neuroendocrine function and contribute to the observed decline in the studied parameter [15,18,19]. In addition, the presence of phytoestrogen-like compounds may help restore hormonal balance through interaction with hormone receptors and neurotransmitter systems within the central nervous system [19].

Table (2) indicates that the study sample was predominantly composed of younger age groups, particularly participants aged 25–34 years, who represented the largest proportion of the sample (40%). A substantial representation was also observed in the 15–24 age group, especially among single women. This demographic distribution is important when interpreting the study outcomes, as several reports suggest that hormonal disorders, including elevated

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prolactin levels and menstrual irregularities, are more prevalent or clinically evident among younger women due to physiological and psychosocial factors characteristic of these life stages [17,30].

Marital status may also indirectly influence symptom severity through its effects on psychological stress, anxiety, similar findings were reported by Abdnezhad et al. [17] and emotional well-being, psychological stress, and anxiety are known to modulate prolactin secretion through the hypothalamic pituitary axis, as reported by Patisaul, who demonstrated that neuroendocrine regulation of prolactin is sensitive to both endogenous and exogenous hormonal signals affecting brain function [20]. Consequently, the higher proportion of single participants may be associated with greater baseline symptom severity, thereby partially explaining the substantial improvement observed following the therapeutic intervention [23].

The findings summarized in Table (3) demonstrate a marked reduction in the prevalence of all reported clinical symptoms after treatment, indicating a comprehensive therapeutic effect on both physical and psychological manifestations. Chest pain decreased from 30% to 10%, menstrual cycle irregularities declined from 52% to 15%, and galactorrhea was reduced from 10% to 2%. Notably, depressive symptoms were completely absent after treatment.

The complete resolution of depressive symptoms is a particularly important outcome, as it suggests a potential modulatory effect of the intervention on central neurotransmitter systems, including dopamine and serotonin, which play key roles in mood regulation as reported by Carr and Lucky [21]. Additionally, the reduction in prolactin levels may have indirectly contributed to psychological improvement, given the established association between hyperprolactinemia and symptoms such as depression, anxiety, and sleep disturbances [22,23].

Improvements in menstrual irregularities and galactorrhea may be attributed to the regulation of prolactin secretion and the influence of phytoestrogenic compounds, which may help rebalance reproductive hormones [20,22]. These findings are consistent with previous studies reporting the beneficial effects of medicinal plants such as *Salvia officinalis*, marjoram, and *Vitex* species on menstrual disorders and prolactin-related symptoms [24].

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When comparing the current clinical findings with experimental studies investigating the effects of plant extracts on prolactin levels in animal models, a consistent trend toward prolactin reduction is observed, despite variations in response depending on sex and extract type. Studies on male rats with induced hyperprolactinemia demonstrated that *Salvia officinalis* and celery seed extracts significantly reduced prolactin levels, with some plant extracts exhibiting greater efficacy than the standard drug bromocriptine [24,25]. In contrast, studies involving female rats revealed differential responses, with marjoram and celery seed extracts showing greater efficiency in reducing prolactin levels compared with *Salvia officinalis*, which exhibited relatively lower efficacy or even a mild increase in some cases. This variation may be explained by the phytoestrogenic content of *Salvia officinalis*, which could interact differently with the endogenous estrogenic environment in females, thereby influencing prolactin regulation as reported by Mohamed et al [24). These findings support the hypothesis that the effects of plant extracts on prolactin secretion are context-dependent and influenced by sex, hormonal status, extract composition, and dosage. This underscores the importance of conducting well-designed clinical studies before generalizing the therapeutic use of such plant-based interventions [17,24,25,26].

Previous research has highlighted the substantial role of the placebo effect in reducing symptom severity, particularly in disorders with strong psychological components, such as premenstrual syndrome and stress-related hormonal disturbances [27,28]. It has been reported that placebo interventions alone may lead to symptom reductions of up to 30% [29]. However, the magnitude of improvement observed in the present study, both in quantitative measures and clinical symptoms, exceeds what can reasonably be attributed to placebo effects alone, suggesting a potential therapeutic benefit of the intervention. Nevertheless, these findings should be interpreted with caution due to certain limitations of the study, including the relatively small sample size, the short duration of the intervention, and the absence of a control group.

CONCLUSION

In conclusion, the findings of the present study demonstrate that the applied therapeutic intervention exerted a significant effect in

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reducing the studied parameter and alleviating associated clinical symptoms, particularly those related to hormonal imbalance and elevated prolactin levels. These results contribute valuable evidence supporting the potential use of plant-based extracts as complementary or alternative therapeutic options, provided that their efficacy is further validated through comprehensive clinical investigations.

Study Limitations and Future Recommendations

Despite the promising results, the present study has several limitations that should be considered when interpreting the findings. These include the absence of a control group, the non-randomized exploratory design, reliance on self-reported clinical assessments, and a relatively small sample size (n = 50). In addition, the short duration of the intervention (two weeks) did not allow the assessment of long-term effects, and the influence of different dosages or formulations of Salvia officinalis was not examined. Therefore, causal relationships cannot be definitively established, and the findings should be interpreted with caution.

Future research should include well-designed randomized controlled trials with larger and more diverse populations, extended follow-up periods, and additional hormonal and biochemical markers. Comparative studies evaluating plant-based interventions against standard pharmacological treatments are also warranted to better define their clinical efficacy and safety.

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