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Effectiveness of Chamomile on Managing Oligomenorrhea in Women with Polycystic Ovary Syndrome: A Double-blind Randomized Clinical Trial

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Abstract

Background: The use of complementary and alternative medicine in managing polycystic ovary syndrome (PCOS) has gained attention due to its potential benefits and fewer side effects compared to conventional treatments. This study aims to assess the effectiveness of chamomile in improving clinical symptoms in women with PCOS, specifically focusing on oligomenorrhea, menstrual cycle regularity, and the presence of dominant follicles.

Materials and Methods: This double-blind randomized clinical trial was conducted on 70 patients diagnosed with PCOS based on the Rotterdam criteria, who were referred to the women's clinic at Imam Reza Hospital in Mashhad, Iran. The subjects were randomly assigned to two equal groups: the intervention group received two 500 mg chamomile capsules daily, while the placebo group received two placebo capsules daily for three months. The response to treatment was evaluated three months post-intervention.

Results: Finally, 60 participants remained in the study, with mean ages of 25.43 ± 5.58 years for the chamomile group and 28.06 ± 5.71 years for the placebo group ($p > 0.05$). In the chamomile group, symptoms of oligomenorrhea decreased following treatment ($p = 0.048$); however, the difference between the two groups was not statistically significant. Notably, 30% of participants in the chamomile group experienced a significant reduction in longer menstrual cycles (over 35 days) ($p = 0.049$), and there was a significant increase in dominant follicles after treatment ($p = 0.02$).

Conclusion: Chamomile treatment significantly reduced symptoms of oligomenorrhea and improved menstrual regularity in the intervention group. One-third of the participants in the chamomile group experienced a significant reduction in longer menstrual cycles (over 35 days), and there was an increase in dominant follicles, suggesting enhanced ovarian function. These findings highlight the potential benefits of chamomile for menstrual health in women with PCOS.

Key Words: Chamomile, Effect, Iran, Polycystic Ovary Syndrome.

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1- INTRODUCTION

Polycystic ovary syndrome (PCOS), historically known as Stein-Leventhal syndrome, is a common endocrine disorder affecting women of reproductive age, with a significantly varying prevalence across different studies and populations. Estimates suggest that PCOS affects 6% to 20% of women globally, which translates to approximately 116 million women, or 3.4% of the female population, according to the World Health Organization (1). PCOS is recognized as the leading cause of anovulatory infertility, accounting for approximately 70% of infertility cases related to ovulation disorders (2, 3).

Polycystic ovary syndrome is a complex endocrine disorder characterized by irregular menstrual cycles, hyperandrogenism, and insulin resistance. Its etiology is multifactorial, involving an intricate interplay of genetic, environmental, and lifestyle factors (4-8). Traditional treatments for PCOS include hormonal contraceptives, anti-androgens, and insulin-sensitizing agents; however, these can have side effects that patients may wish to avoid. The use of complementary medicine for treating PCOS has gained attention due to its holistic approach and potential benefits. Various modalities, including traditional Chinese medicine (TCM), homeopathy, nutraceuticals, and medicinal plants, offer alternative strategies to effectively manage PCOS symptoms (9-14).

Chamomile (Matricaria chamomilla) has garnered attention for its potential therapeutic effects on polycystic ovary syndrome (PCOS). Its anti-inflammatory properties and ability to modulate hormonal levels, particularly testosterone, make it a promising herbal treatment for managing symptoms associated with PCOS (15, 16). Research on animal models has demonstrated that chamomile can improve ovarian morphology by reducing cyst formation and increasing the number of dominant follicles. Studies involving rats with induced PCOS indicated that chamomile treatment resulted in significant histological improvements in ovarian tissue, including a reduction in cysts and enhanced follicular development (17). The present trial explores the potential benefits of chamomile as a natural treatment for managing symptoms of polycystic ovary syndrome, with a focus on oligomenorrhea, menstrual cycle regularity, and the development of dominant follicles. The findings may enhance the understanding of alternative therapies for women with this common endocrine disorder.

2- MATERIALS AND METHODS

2-1. Study Design and Methodology

This randomized double-blind clinical trial involved 70 patients diagnosed with PCOS, divided into two groups of 35 participants each: an intervention group and a placebo group. The study utilized a convenience sampling technique, selecting subjects from referrals to the gynecological clinic of Imam Reza Hospital in Mashhad, Iran, from 2017 to 2018. After outlining the study objectives and addressing ethical considerations in accordance with the Helsinki Declaration, written consent was obtained from all participants, ensuring the confidentiality of their information. Participants were informed that they could withdraw from the study at any time if they chose not to continue.

A questionnaire capturing demographic variables was administered to the participants. Subsequently, patients were asked to visit Imam Reza Hospital for a transvaginal ultrasound on days three to five of their menstrual cycle. Patients experiencing amenorrhea were advised to come for the ultrasound after experiencing bleeding, which could be induced by taking 10 mg of progesterone daily for

seven days. Upon referral to the gynecological clinic of Imam Reza Hospital, patients presented their ultrasound results and biochemical test findings. If diagnosed with PCOS, they were randomly assigned to either the intervention group or the control group following confirmation of their condition through ultrasound and biochemical tests. Outcome measures for this study included changes in clinical symptoms associated with PCOS, specifically focusing on oligomenorrhea, menstrual cycle regularity, and the development of dominant follicles.

2-2. Sample Size Calculation

The initial sample size was calculated using PASS software, which determined that 31 participants were needed in each group. However, the final sample size was adjusted to 35 participants per group to enhance the statistical power of the study.

2-3. Rotterdam Criteria

Initially, the obstetrician-gynecologist ruled out other disorders that mimic the PCOS phenotype, including hyperprolactinemia, thyroid dysfunction, Cushing's syndrome, congenital adrenal hyperplasia, and androgen-secreting ovarian tumors. Next, polycystic ovary syndrome was diagnosed using the Rotterdam criteria (18), which require at least two of the following three conditions:

- Oligo-ovulation or anovulation: Irregular menstrual cycles, such as oligomenorrhea (fewer than six to nine periods per year) or amenorrhea (absence of menstruation).
- Hyperandrogenism: This can manifest as clinical signs like hirsutism or elevated androgen levels in blood tests.
- Polycystic ovaries on ultrasound: Defined by having at least 12 antral follicles in one ovary or an ovarian volume larger than 10 cm^3.

2-4. Inclusion Criteria

- Women's reproductive age.
- History of normal puberty
- Suffering from dysmenorrhea
- Diagnosis of PCOS according to the Rotterdam criteria
- Normal thyroid function tests
- No recent history of surgery or treatment for PCOS
- No use of hormonal medications, herbal medicines, or smoking
- Having a BMI < 30 kg/m^2.

2-5. Exclusion Criteria

- Recent use of sex steroids (such as birth control pills, hormone therapy, or androgenic drugs)
- Use of chemical or herbal medications
- Tobacco use
- Thyroid disorders
- Recent surgical treatment for PCOS
- History of treatment for Polycystic Ovary Syndrome.

2-6. Interventions

Chamomile capsules are available in the Iranian pharmaceutical market and are derived from the hydroalcoholic extract of the chamomile plant, Matricaria chamomilla. Each capsule contains 500 mg of chamomile extract standardized to 1.2% apigenin. The placebo capsules used in the study were manufactured by the Mashhad Faculty of Pharmacy. The capsules were provided to the patients based on a checklist. The effective dose was determined to be 500 mg according to previous studies. Chamomile capsules used in the study were produced by Barij Essence Pharmaceutical Company in Iran. The intervention group received two capsules per day for three months, while the control group received two placebo capsules per day for the same duration. An individual unrelated to the study packaged and numbered the drugs. Chamomile and placebo capsules, which were identical in appearance, were placed in two envelopes

labeled A and B. For each patient, a site coordinator randomly selected an envelope. Both the facilitators and patients were unaware of the contents of the envelopes. On day 12 of the third cycle, and in cases of amenorrhea at the end of day 90, subjects were referred for transvaginal sonography to evaluate the drug's effect on ovarian volume and follicle development using vaginal ultrasound (5 MHz Ultramark 4 Plus; Advanced Technology Laboratories, Bothell, WA).

2-7. Data Collection and Measurement

A questionnaire was developed to assess socio-demographic and clinical features, including age, marital status, weight, height, body mass index (BMI), pregnancy history, history of infertility, and oligomenorrhea. Information regarding oligomenorrhea was collected three months post-intervention, with a researcher responsible for completing the checklists. Height was measured in a standing position without shoes using a wall-mounted tape measure, recorded to the nearest 0.5 cm. Weight was measured with a Secca scale (manufactured in Germany), without shoes and while wearing light clothing, recorded to the nearest 0.1 kg. The body mass index was calculated by dividing weight (in kilograms) by height (in square meters).

2-8. Ethical Considerations

This randomized double-blind clinical trial adhered to the ethical principles of the Declaration of Helsinki and received approval from the Ethics Committee of Mashhad University of Medical Sciences (IR.MUMS.fm.REC.1396.444). Written informed consent was obtained from all participants, ensuring confidentiality and the right to withdraw at any time. The protocol included protective measures for participant welfare during procedures such as transvaginal ultrasound, with clear disclosure of potential risks. Ethical accountability was reinforced through transparency about placebo use, post-study care, and robust data protection. The study also respected Iranian cultural considerations in women's health. While prospective trial registration was not conducted—consistent with practices in Iran at that time—all ethical standards were met through institutional review board approval.

2-9. Statistical Analysis

The data were analyzed using SPSS software version 23. Descriptive statistics, including measures of central tendency, dispersion, and frequency distribution, were employed to present the characteristics of the subjects. For normally distributed quantitative variables, an independent t-test was conducted, while the Mann-Whitney test was utilized for non-normally distributed data. To compare qualitative variables, both the chi-square test and Fisher's exact test were applied. Additionally, McNemar's test was used to assess changes in paired nominal data, particularly focusing on clinical symptoms such as menstrual cycles before and after treatment within the intervention group. A p-value of ≤ 0.05 was considered statistically significant.

3- RESULTS

A total of 70 patients were randomly assigned to either an intervention group or a placebo group, with each group consisting of 35 participants. However, several patients were excluded from the analysis during the study. Two patients in the intervention group were removed due to gastrointestinal complications, and three were excluded for not adhering to the prescribed drug regimen. In the placebo group, five patients were excluded for similar reasons related to incomplete drug use. Ultimately, data from 60 patients were analyzed, with 30 in the intervention group and 30 in the placebo group (**Figure 1**).

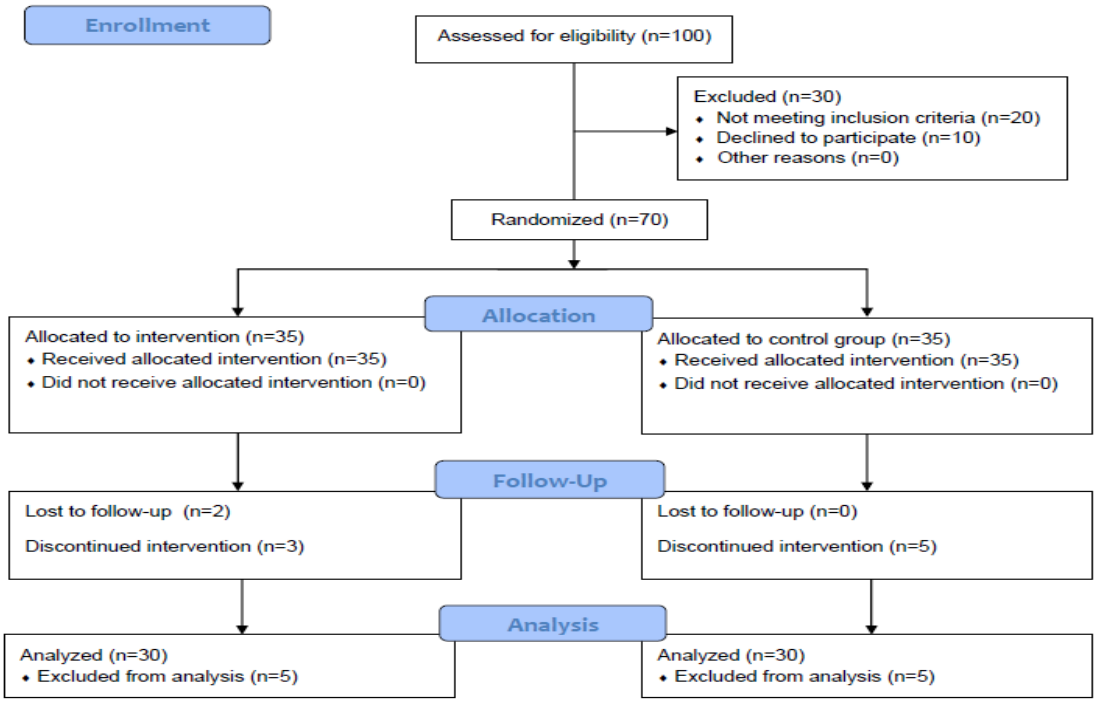

Figure 1. CONSORT Flow Diagram.

The following data highlight key comparisons in demographics, medical histories, and menstrual cycle characteristics, providing insight into the efficacy of the treatment:

The mean age of the patients was 25.43 ± 5.58 years in the intervention group and 28.06 ± 5.71 years in the placebo group. The number of individuals under 18 was higher in both groups; however, this difference was not statistically significant. The mean age, BMI, marital status, and histories of pregnancy and infertility were similar between the two groups before treatment (**Table 1**). Before treatment, the BMI was 25.28 ± 4.98 in the intervention group and 25.58 ± 5.98 in the placebo group. The independent samples t-test indicated no significant difference between the two groups (p = 0.831) (**Table 1**). Additionally, there was no statistically significant difference in BMI between the chamomile group (25.17 ± 4.95), and the placebo group (25.57 ± 6.70) after treatment (p=0.777).

Table 1: Pre-intervention Comparison of Demographic and Medical History between Intervention and Placebo Groups (n = 60).

Variable	P-value	Intervention Group (Number, %)	Placebo Group (Number, %)
Marital Status	0.436*	Married: 18 (60)	Married: 12 (40)
		Single: 15 (50)	Single: 15 (50)
Pregnancy History	0.898*	Yes: 8 (44.4)	Yes: 7 (46.7)
		No: 22 (55.6)	No: 23 (53.3)
History of Infertility	>0.99*	Yes: 3 (16.7)	Yes: 2 (13.3)
		No: 27 (83.3)	No: 28 (86.7)
Age, year	0.2*	≤18 years: 18 (60)	≤18 years: 17 (56.7)
		>18 years: 12 (40)	>18 years: 13 (43.3)
Pre-treatment BMI	0.831**	25.28 ± 4.98	25.58 ± 5.98

*Chi-Square, **Independent t-test, BMI: Body Mass Index.

Table 2: Comparison of clinical symptoms, specifically oligomenorrhea, before and after treatment in the intervention group (n = 30).

Variable	P-value	Intervention Group, n=30 (Number, %)	Placebo Group, n=30 (Number, %)
Oligomenorrhea			
Less than 35 days	0.071*	19 (63.3%)	18 (60%)
More than 35 days	0.069*	10 (33.3%)	17 (56.7%)
Intragroup p-values			
Less than 35 days	0.99*	-	-
More than 35 days	0.049*	-	-

*Chi-Square test.

Table 2 compares oligomenorrhea between the intervention and placebo groups, each consisting of 30 participants. In cycles shorter than 35 days, the intervention group had 19 participants with oligomenorrhea (63.3%) compared to 18 participants (60%) in the placebo group, with a p-value of 0.071, indicating no significant difference. For cycles longer than 35 days, the intervention group had 10 participants (33.3%) versus 17 participants (56.7%) in the placebo group, with a p-value of 0.069, also showing no significant difference. However, the intragroup analysis revealed a significant change for cycles longer than 35 days ($p = 0.049$) within the intervention group, suggesting that the intervention may help reduce longer menstrual cycles, even though overall differences between groups were not statistically significant. This indicates that after the intervention in the chamomile group, the number of participants with oligomenorrhea decreased significantly to 30% ($p < 0.05$).

Table 3: Comparison of clinical symptoms, specifically menstrual cycles, before and after treatment in the intervention group (n = 30).

Menstruation Status		Menstruation After Treatment		Total participants	P-value
		(35 days or fewer)	(35 days or more)		
Before Treatment	(35 days or fewer)	7 (63.6%)	4 (36.4%)	11	0.049*
	(35 days or more)	13 (68.4%)	6 (31.6%)	19	
Total		20	10	30	

*McNemar Test.

Table 3 compares the menstrual cycle status of 30 participants before and after treatment, analyzed using McNemar's test. The results indicate a significant change, with a p-value of 0.049, suggesting that the treatment likely improved menstrual cycle regularity. Specifically, 60% of participants who had cycles of 35 days or fewer before treatment continued to have similar cycles afterward, while 40% shifted to longer cycles. In contrast, only 30% of participants with cycles longer than 35 days before treatment remained in that category after treatment, indicating a trend toward shorter cycles. Overall, these findings suggest that the intervention may effectively enhance menstrual cycle regularity.

Table 4: Comparison of clinical symptoms, specifically menstrual cycles, before and after treatment in the placebo group (n = 30).

Menstruation Status		Menstruation After Treatment		Total participants	P-value
		(35 days or fewer)	(35 days or more)		
Before Treatment	(35 days or fewer)	6 (50.0%)	6 (50.0%)	12	0.99*
	(35 days or more)	7 (38.9%)	11 (61.1%)	18	
Total		13	17	30	

*McNemar Test.

Table 4 compares the menstrual cycle status before and after treatment in the placebo group, which included 30 participants, analyzed using McNemar's test. Among those with cycles of 35 days or fewer before treatment, 50% remained in that category afterward, while the other half transitioned to longer cycles. For participants who initially had cycles longer than 35 days, only 38.9% experienced shorter cycles post-treatment, while 61.1% continued to have longer cycles. The p-value of 0.99 indicates no statistically significant change in menstrual patterns, suggesting that the placebo had no observable effect on cycle regularity.

Table 5: Comparison of dominant follicles between the placebo and intervention groups.

Characteristics	Intervention (n=30)	Placebo (n=30)	P-value
Dominant Follicles Before Treatment			
No	27 (90%)	28 (93.3%)	0.579*
Mono	0 (0%)	2 (6.7%)	
Multi	3 (10%)	0 (0%)	
Dominant Follicles in the First Cycle			
No	25 (83.3%)	28 (93.3%)	0.184*
Mono	0 (0%)	2 (6.7%)	
Multi	5 (16.7%)	0 (0%)	
Dominant Follicles in the Third Cycle			
No	15 (50%)	21 (70%)	0.027*
Mono	6 (20%)	9 (30%)	
Multi	9 (30%)	0 (0%)	

*Mann Whitney U test.

Table 5 presents the analysis of dominant follicles before treatment and on day 12 of the first and third cycles, using the Mann-Whitney U test. A significant difference was observed in the number of dominant follicles between the two groups in the third cycle, with the intervention group exhibiting a higher count (p = 0.027).

4- DISCUSSION

This study assessed the effectiveness of chamomile in improving symptoms in women with PCOS, focusing on oligomenorrhea, menstrual cycle regularity, and dominant follicles. The results indicated that chamomile significantly reduced symptoms of oligomenorrhea and decreased the number of menstrual cycles longer than 35 days. Additionally, there was a notable increase in the number of dominant follicles after treatment, suggesting that chamomile may enhance ovarian function and promote ovulation in women with PCOS. However, no statistically significant difference in BMI was observed between the chamomile group and the placebo group post-treatment.

Polycystic ovary syndrome is a prevalent endocrine disorder characterized by hormonal imbalances, with symptoms such as irregular menstrual cycles (oligo-/amenorrhea), hirsutism, and infertility (19-21). Traditional treatments often involve hormonal contraceptives or insulin-sensitizing agents, which may have side effects that patients wish to avoid (22, 23). Given the complexity of PCOS, treatment approaches have continuously evolved. Recent interest has focused on herbal medicine as a complementary or alternative therapy to conventional treatments (24). Herbal medicine is a promising approach for managing PCOS symptoms due to its potential efficacy and lower side effects compared to synthetic drugs. Research indicates that various herbs, such as inositol, Stachys lavandulifolia (Iranian wild mint), black cohosh, ginseng, aloe vera, and chamomile, can help alleviate symptoms associated with PCOS by targeting hormonal imbalances and metabolic issues (25-27).

The effectiveness of chamomile in managing oligomenorrhea among women with PCOS has been explored in several studies, indicating promising results. Recent reviews highlight chamomile as an effective herbal treatment for conditions such as oligo-/amenorrhea, offering a safer alternative to conventional treatments that may carry adverse effects (28). One study titled "The Effect of Chamomile on Menstrual Patterns and Serum Androgens in Polycystic Ovary Syndrome" found that chamomile significantly improved menstrual regulation in women with PCOS. Specifically, there was a notable increase in normal menstrual cycles ($p<0.001$), and a reduction in testosterone levels among participants, indicating the effectiveness of chamomile in addressing oligomenorrhea and hyperandrogenism associated with PCOS. These findings suggest that chamomile may be a beneficial natural treatment option for managing symptoms of this condition (16).

Another study investigated the effect of chamomile capsules on hormonal and lipid parameters in women with PCOS and found that chamomile significantly reduced total testosterone levels but did not affect lipid profiles or other hormonal parameters. Although the study did not directly assess its impact on symptoms such as oligomenorrhea, it underscores the need for further research to explore the potential benefits of chamomile for ovarian function and the overall management of PCOS (29).

A recent study by Heidary et al. (2022) with 80 participants found a significant increase in the number of women achieving normal menstrual cycles after treatment, demonstrating statistical significance ($p < 0.001$). This suggests that the treatment may effectively address menstrual irregularities and highlights the need for further research on its long-term effects and mechanisms (16). Another study on chamomile extract in a rat model of PCOS found that it significantly stimulated menstruation and improved ovarian function. Treatment led to fewer follicular cysts and an increase in dominant follicles, along with enhanced luteinizing hormone (LH) levels. These results suggest that chamomile may help manage oligomenorrhea in women with PCOS, but further research in humans is needed to confirm its effectiveness (17).

These findings suggest that chamomile could be a promising herbal remedy for women experiencing hormonal disorders, warranting further investigation into its long-term efficacy (29). Chamomile has demonstrated potential benefits for managing oligomenorrhea in women with PCOS, but further large-scale studies are essential to validate these findings and clarify the mechanisms of action involved. Some research indicates that although chamomile may assist in regulating

menstrual cycles, it does not significantly influence all hormonal parameters, highlighting the necessity for comprehensive treatment strategies (30).

Based on the current results, a significant difference was observed in the number of dominant follicles during the third cycle between the two groups, with the intervention group showing a higher count. This finding indicates that the intervention effectively enhances follicular development, highlighting its potential benefits in fertility treatments. Furthermore, this result is consistent with existing literature on ovarian stimulation and follicle dynamics (31, 32). The clinical implications of these findings are substantial, as an increase in dominant follicles can improve the chances of successful ovulation and subsequent pregnancy outcomes. Additionally, research has demonstrated that manipulating the ovarian environment through stimulation protocols can lead to better results in assisted reproductive technologies. For instance, studies have shown that the ablation of larger follicles can elevate circulating follicle-stimulating hormone (FSH) levels, promoting the growth of remaining follicles (32-34).

The finding that no statistically significant difference in BMI was observed between the chamomile and placebo groups post-treatment suggests that while chamomile may alleviate certain symptoms of PCOS, it does not directly affect weight management. This aligns with previous studies indicating that chamomile can improve clinical symptoms such as hirsutism but may not significantly influence metabolic parameters or overall BMI (15, 35). The lack of change in BMI could reflect the complexity of PCOS, where hormonal imbalances and lifestyle factors often play a more substantial role in weight than herbal interventions alone. Therefore, while chamomile shows promise as a supportive treatment for managing specific symptoms of PCOS, it should be considered as part of a broader approach that includes lifestyle modifications for effective weight management (35).

This study suggests chamomile as a simple, cost-effective adjunct therapy for PCOS women. Further research is needed to confirm results and elucidate mechanisms, but initial evidence indicates potential to improve reproductive health via enhanced follicular development and menstrual cycle regulation.

4-1. Study Limitations and Suggestions

This study on chamomile's effects on oligomenorrhea has limitations: small sample size (60 participants, 30/group) limiting statistical power and generalizability; short three-month duration missing long-term effects; high dropout rate; and lack of prospective registry registration (consistent with Iranian practices then), despite full Ethics Committee approval. Future studies should prioritize larger samples, longer follow-ups, dropout mitigation, and prospective registration for enhanced transparency.

5- CONCLUSION

Chamomile supplementation demonstrates preliminary benefits in alleviating oligomenorrhea among women with polycystic ovary syndrome (PCOS), including symptom reduction and increased dominant follicle counts. These effects appear independent of body mass index (BMI) changes, suggesting a direct influence on menstrual regulation. However, the absence of significant differences versus placebo underscores methodological limitations and necessitates larger, randomized controlled trials.

Future research should prioritize long-term outcomes, dose optimization, and mechanistic studies (e.g., hormonal

pathways) to validate chamomile's efficacy. Until then, it may serve as a complementary option alongside conventional PCOS management, pending robust evidence.

6- CONFLICT OF INTEREST: None.

7- REFERENCES

1. Różańska-Smuszkiewicz, Gabriela, Smuszkiewicz-Różański, Paweł, Kmiotek, Weronika, Ragan, Dagmara, Oronowicz, Radosław, Staszczak, Paweł, Jaworska, Barbara, Długosz, Joanna, Bara, Maciej and JAMA, Grzegorz. The influence of physical activity, diet, and lifestyle of patients on the course of polycystic ovary syndrome (PCOS) in women. Quality in Sport. 2024; 19: 53209. https://dx.doi.org/10.12775/QS.2024.19.53209.

2. Cunha A, Póvoa AM. Infertility management in women with polycystic ovary syndrome: a review. Porto Biomed J. 2021 Jan 26;6(1):e116. doi: 10.1097/j.pbj.0000000000000116. PMID: 33532657; PMCID: PMC7846416.

3. Hoyt KL, Schmidt MC. Polycystic ovary (Stein-Leventhal) syndrome: etiology, complications, and treatment. Clin Lab Sci. 2004 Summer;17(3):155-63. PMID: 15314890.

4. Atiomo, W., Rizwan, M. N. H., Bajwa, M. H., Furniturewala, H. J., Hazari, K. S., Harab, D., Abdelkareem, W., Inuwa, S., Khamis, A. H., Tahlak, M., & Mirza, F. G. Prevalence and Diagnosis of PCOS Using Electronic Health Records: A Scoping Review and a Database Analysis. International Journal of Environmental Research and Public Health, 2024; 21(3): 354. https://doi.org/10.3390/ijerph21030354.

5. Sajjan, Iqbal, Memon., Misbah, Shakeel., Hannah, Syed., Khalid, Amin., Aya, A., Khalil., Maryam, Sulaiman. Prevalence, Risk Factors and Management of Polycystic Ovary Syndrome: A Review with Current Evidence. Iraq medical journal, 2024;8(1). doi: 10.22317/imj.v8i1.1268.

6. M., Amin., Claudia, Gragnoli. Genome-wide linkage and association study identifies novel genes and pathways implicated in polycystic ovarian syndrome.. European Review for Medical and Pharmacological Sciences, 2023;27 8(8):3719-32. doi: 10.26355/eurrev_202304_32171.

7. Manuela, Silva., Rodrigo, Vargas. Fetal metabolic programming in the etiology of polycystic ovarian syndrome. Contemporânea, 2023;3(8):10436-450. doi: 10.56083/rcv3n8-028.

8. Vijay, Daulatrao, Havaldar., Nilam, Yuvraj, Jadhav., Snehal, Shashikant, Shinde., Savita, Shivaji, Mali., Kailas, Krishnat, Mali., Aishwarya, Atmaram, Shinde., Rutuja, Amarsing, Rajput. A review on PCOS: Its causes, symptoms, pathogenesis and management. World Journal of Advanced Pharmaceutical and Medical Research, 2024, 07(01):014–021. doi: 10.53346/wjapmr.2024.7.1.0041

9. Domecq JP, Prutsky G, Mullan RJ, Sundaresh V, Wang AT, Erwin PJ, Welt C, Ehrmann D, Montori VM, Murad MH. Adverse effects of the common treatments for polycystic ovary syndrome: a systematic review and meta-analysis. J Clin Endocrinol Metab. 2013 Dec;98(12): 4646-54. doi: 10.1210/jc.2013-2374. Epub 2013 Oct 3. PMID: 24092830; PMCID: PMC5399491.

10. Fu LW, Gao Z, Zhang N, Yang N, Long HY, Kong LY, Li XY. Traditional Chinese medicine formulae: A complementary method for the treatment of polycystic ovary syndrome. J Ethnopharmacol. 2024 Apr 6;323:117698. doi: 10.1016/j.jep.2023.117698. Epub 2024 Jan 1. PMID: 38171464.

11. V., K., Jayasree. An Initial Exploration of Homoeopathic Medicines Effectiveness in Treating PCOS: A Pilot Study. Psychology & psychological research international journal, 2024.;9(2):1-3. doi: 10.23880/pprij-16000416.

12. Scannell N, Mantzioris E, Rao V, Pandey C, Ee C, Mousa A, Moran L, Villani A. Type and Frequency in Use of Nutraceutical and Micronutrient Supplementation for the Management of Polycystic Ovary Syndrome: A Systematic Scoping Review. Biomedicines. 2023 Dec 18;11(12):3349. doi: 10.3390/biomedicines11123349.

13. S Prema, Firoj A Tamboli, Bhupinder Bhyan, Hanish Singh Jayasingh Chellammal. Development and Evaluation of Polyherbal

Phyto-phospholipid Complexes (Phytosomes) for PCOD Treatment. International journal of drug delivery technology, 2024;14(02):853-57. doi: 10.25258/ijddt.14.2.37

14. Jiao B, Chen R, Chen S, Zhang J, Wang P, Zhou H, Zhao W. Plant medicine metabolite Yulinzhu treating neurological disorder causing polycystic ovary syndrome: a systematic review and a meta-analysis. Front Pharmacol. 2024 Aug 15;15:1458621. doi: 10.3389/fphar.2024.1458621.

15. Malihe Afiat , Naghmeh Khorsand , Azam Akbari Lor, Mona Najaf Najafi, Masumeh Ghazanfarpour. Evaluating the Effect of Chamomile on Ovulation Induction in Women with Polycystic Ovary Syndrome: A Clinical Trial. International Journal of Women's Health and Reproduction Sciences, 2025. doi: 10.15296/ijwhr.2023.31.

16. Maryam, Heidary., Sara, Dokuhaki., Zahra, Yazdanpanahi., Mohammad, Hossein, Dabbaghmanesh., Masoumeh, Emamghoreishi., Marzieh, Akbarzadeh. The effect of chamomile on menstruation pattern and serum androgens in polycystic ovary syndrome. Medicinal Plants - International Journal of Phytomedicines and Related Industries, 2022;14(1):64-71. doi: 10.5958/0975-6892.2022.00007.7

17. Farideh ZZ, Bagher M, Ashraf A, Akram A, Kazem M. Effects of chamomile extract on biochemical and clinical parameters in a rat model of polycystic ovary syndrome. J Reprod Infertil. 2010 Oct;11(3):169-74.

18. Franks S. Controversy in clinical endocrinology: diagnosis of polycystic ovarian syndrome: in defense of the Rotterdam criteria. J Clin Endocrinol Metab. 2006;91(3):786-89. doi:10.1210/jc.2005-2501.

19. Khalesi ZB, Beiranvand SP, Bokaie M. Efficacy of Chamomile in the Treatment of Premenstrual Syndrome: A Systematic Review. J Pharmacopuncture. 2019 Dec;22(4):204-209. doi: 10.3831/KPI.2019.22.028. Epub 2019 Dec 31. PMID: 31970017; PMCID: PMC6970572.

20. Alev Onder, Ozge Yilmaz, Ahsen Sevde Cinar Koc and Harun Kizilay. Medicinal Plants including Spices for the Treatment of Polycystic Ovary Syndrome (PCOS) with a Preclinical-Clinical Perspective and Phytotherapeutic Approaches. 2024;1-45. doi: 10.2174/9789815196801124030003.

21. Nan, Liu., Hongli, Zhu. Progress of Chinese and Western Medicine Research on Polycystic Ovary Syndrome. Journal of Contemporary medical practice, 2024;6(6):79-85. doi: 10.53469/jcmp.2024.06(06).14.

22. Jiawen Dong, D Aled Rees - Polycystic ovary syndrome: pathophysiology and therapeutic opportunities: BMJ Medicine 2023;2:e000548.

23. Singh S, Pal N, Shubham S, Sarma DK, Verma V, Marotta F, Kumar M. Polycystic Ovary Syndrome: Etiology, Current Management, and Future Therapeutics. J Clin Med. 2023 Feb 11;12(4):1454. doi: 10.3390/jcm12041454.

24. Vaishnavi, Gadage., Rohan, Dhute., Pratik, Choukhande., Aniket, Dalvi., Sakshi, Dhamne. A Review on PCOD: Polycystic Ovarian Disease. International Journal of Advanced Research in Science, Communication and Technology, (2024). doi: 10.48175/ijarsct-17858.

25. Manouchehri A, Abbaszadeh S, Ahmadi M, Nejad FK, Bahmani M, Dastyar N. Polycystic ovaries and herbal remedies: A systematic review. JBRA Assist Reprod. 2023 Mar 30;27(1):85-91. doi: 10.5935/1518-0557.20220024.

26. Kwon CY, Cho IH, Park KS. Therapeutic effects and mechanisms of herbal medicines for treating polycystic ovary syndrome: A review. Frontiers in pharmacology. 2020 Aug 12;11:1192.

27. Lakshmi JN, Babu AN, Kiran SSM, Nori LP, Hassan N, Ashames A, Bhandare RR, Shaik AB. Herbs as a Source for the Treatment of Polycystic Ovarian Syndrome: A Systematic Review. BioTech (Basel). 2023 Jan 3;12(1):4. doi: 10.3390/biotech12010004.

28. Ashkar F, Rezaei S, Salahshoornezhad S, Vahid F, Gholamalizadeh M, Dahka SM, Doaei S. The Role of medicinal herbs in treatment of insulin resistance in patients with Polycystic Ovary Syndrome: A literature review. Biomol Concepts. 2020 Mar 26;11(1):57-75. doi: 10.1515/bmc-2020-0005.

29. Heidary M, Yazdanpanahi Z, Dabbaghmanesh MH, Parsanezhad ME, Emamghoreishi M, Akbarzadeh M. Effect of chamomile capsule on lipid- and hormonal-related parameters among women of reproductive age with polycystic ovary syndrome. J Res Med Sci. 2018 Apr 26;23:33. doi: 10.4103/jrms.JRMS_90_17.

30. Abbasi E, Hajhashemy Z, Askari G, Saneei P. Association of Herbal Tea and Follicle-Stimulating Hormone, Anthropometric Parameters, and Fasting Blood Glucose Levels Among Polycystic Ovarian Syndrome Women: A Systematic Review and Meta-Analysis of Clinical Trials. Clin Nutr Res. 2024 Jul 30;13(3):201-213. doi: 10.7762/cnr.2024.13.3.201. PMID: 39165287.

31. Li JH, Sun TC, Zhang SW, Jiao TT, Cheng YB, Dong P, Chian RC, Xu Y. Effect of dominant follicle status at the time of retrieval on the clinical outcomes in natural cycle IVF combined with immature oocyte treatment. Aging (Albany NY). 2022 Jun 7;14(11):4728-4738. doi: 10.18632/aging.204106.

32. Huang C, Shen X, Yan Y, Shan H, Shi Q, Mei J, Xing J. The relationship between dominant follicle development and clinical outcomes of hormone replacement therapy-frozen embryo transfer: a retrospective clinical study. Front Endocrinol (Lausanne). 2023 Jun 14;14:1192696. doi: 10.3389/fendo.2023.1192696.

33. Femke Hohmann. Aspects of Mono- and Multiple Dominant Follicle Development in the Human Ovary. Thesis Erasmus University, Rotterdam, The Netherlands, 2005.

34. Ghomian, N., Khosravi, A., Mousavifar, N. A Randomized Clinical Trial on Comparing The Cycle Characteristics of Two Different Initiation Days of Letrozole Treatment in Clomiphene Citrate Resistant PCOS Patients in IUI Cycles. International Journal of Fertility and Sterility, 2015; 9(1): 17-26. doi: 10.22074/ijfs.2015.4204.

35. Afiat M, Akbari Lor A, Najaf Najafi M, Ghazanfarpour M, Jafarabadi M. Examining the Effect of Chamomile on Clinical Symptoms and Hormonal Parameters Among Patients With Polycystic Ovarian Syndrome. J Family Reprod Health. 2022 Dec;16(4):248-253. doi: 10.18502/jfrh.v16i4.11355.