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# The Effectof HypericumPerforatum on Mitigating Premenstrual Syndrome (PMS) Symptoms: A Double-Blind Clinical Trial

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**Abstract**

**Objective:** The primary objective of this study was to examine the effect of HypericumPerforatum on mitigating premenstrual syndrome symptoms in comparison to a placebo among female patients seeking treatment at the Apadana Clinic in Yasuj City.

**Method:** The present study comprised double-blind clinical research involving 105 Iranian women diagnosed with premenstrual syndrome (PMS). These participants were selected through random selection and subsequently assigned to two groups, namely HypericumPerforatum, and placebo, using random categorization. The Premenstrual Symptoms Screening Questionnaire (PSST), which has been standardized for Persian speakers, was employed for data collection. The repeated measures statistical method was employed in this study due to the inclusion of two distinct groups and the implementation of three assessments: pre-test, post-test, and follow-up. The data analysis was conducted using SPSS version 26.

**Results:** The results of the present study revealed that there was no statistically significant difference ($P>0.05$) in the demographic factors between the two groups. Furthermore, the analysis of the data revealed that Perforan, in comparison to the placebo, exhibited a statistically significant reduction in the severity of symptoms associated with premenstrual syndrome ($F=4.041$, $P<0.05$). Additionally, the statistical analysis revealed that both the effect of time ($P<0.05$, $F=29.189$) and the interaction effect between groups and time on the severity of premenstrual syndrome (PMS) symptoms are statistically significant ($P<0.05$, $F=5.825$).

**Conclusion:** The results of the present study indicate that the administration of Perforan leads to a reduction in the severity of premenstrual syndrome (PMS) symptoms when compared to a placebo. Nevertheless, the limited number of clinical trials conducted in this particular domain necessitates further investigation and research.

**Keywords:** Hypericum Perforatum, Perforant, PMS, Symptoms

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## Introduction

Premenstrual syndrome (PMS) is a prevalent disease that is frequently associated with menstruation in women (1). Premenstrual syndrome (PMS) encompasses a range of physiological, psychological, and behavioral manifestations (2) that notably impair the well-being and occupational performance of women during the luteal phase (1), with these symptoms typically subsiding or ceasing upon the commencement of menstruation (3). Premenstrual syndrome (PMS) is commonly categorized into three levels of symptom severity: mild, moderate, and severe. Notably, individuals experiencing severe PMS may exhibit symptoms that resemble those of major depression, leading to an exacerbation of depressive manifestations (4). The prevailing psychological symptoms encompass a low mood, irritability, mood fluctuations, and diminished concentration. Typical physical manifestations encompass widespread bodily pain, headache, backache, fatigue, and articular pains. The study identified several prevalent behavioral effects, including irritability, increased appetite, and excessive drowsiness (5).

The incidence of this condition varies across different countries. According to a study conducted in Iran, the reported prevalence of this particular disease among female high school students was approximately 40% (6). The published figures indicate that in India, the percentage of women affected was 86% (5), while in India 86% (5), America 73% (7), Arab women (Egypt, Syria, and Libya) between 66 and 77% (8) and in Ethiopia 37% (9). A study conducted on a diverse group of international students studying in China, originating from 45 different countries, revealed that approximately 19% of female participants experienced alterations in their menstrual symptoms. This phenomenon may be attributed to factors such as inadequate cultural adaption, diminished sleep quality, heightened stress levels, and limited exposure to life experiences overseas (10). The etiology of premenstrual syndrome (PMS) remains incompletely known. In addition to the previously described influences of cultural and social aspects, physiological and genetic variables have also been implicated in the development of this condition (11, 12, 13, 14, 15). Women place a high premium on the availability of effective therapies with few side effects due to the detrimental implications of menstruation disorders on their quality of life, interpersonal relationship, employment prospects, and women's concerns regarding their menstrual disorders (16). Due to fewer adverse effects than chemical medications, the desire to use herbal medicines has grown in recent years.

One example of such a plants is St. John's wort, which is taxonomically identified as Hypericumperforatum. Hypericumperforatum is a botanical species belonging to the Hyperiacea family. It is indigenous to Western Europe, Asia, and North Africa (17). The plant under consideration possesses a diverse array of flavonoids, hypericin, and prenylated phloroglucinols, including hyperforin (18). Hypericumperforatum possesses potent antioxidant properties, which can be ascribed to the presence of flavonoids and phenolic acids (19). Hypericumperforatum is also recognized for its therapeutic potential in the management of depressive disorders. According to prior research, it appears that hypericin and its derivative, hyperforin, namely phloroglucinol derivative, are likely the primary active constituents responsible for the antidepressant effects (18, 20, 21). The effect of hyperforin is seen by the inhibition of serotonin, norepinephrine, and dopamine reuptake. Additionally, hyperforin is involved in the inhibition of γ-aminobutyric acid (GABA) and L-glutamate reuptake. In addition to its established antidepressant effects, hyperforin has been found to possess anti-anxiety properties, cognitive-enhancing capabilities, and antioxidant properties (20). A study demonstrated the efficacy of HypericumPerforatum in mitigating symptoms associated with premenstrual syndrome (PMS). According to the findings of this study, it is suggested that the consumption of this herb should be continued for a minimum duration of two months specifically during the luteal phase (22). The findings of another study demonstrated that HypericumPerforatum was linked to a reduction in the prevailing physical and behavioral symptoms commonly associated with premenstrual syndrome (PMS) in comparison to a placebo. However, the levels of cytokines did not exhibit any significant differences between the treatment group and the placebo group following the intervention. Furthermore, HypericumPerforatum was found to be ineffective in alleviating mood symptoms and pain associated with PMS (23). In a separate investigation employing perforan tablets (280 mg Hypericumperforatum per day), it was demonstrated that perforan possesses the capacity to mitigate the physical and behavioral manifestations associated with premenstrual syndrome (PMS) throughout the course of one, two, and three months (24). The findings of the study indicate that the administration of HypericumPerforatum, Vitamin E, and Vitex agnus resulted in a reduction in the intensity of premenstrual syndrome (PMS) symptoms. However, it was seen that Vitex agnus exhibited superior efficacy compared to the other two therapies (25). In contrast, the findings of a study demonstrated that HypericumPerforatum did not exhibit efficacy in mitigating premenstrual syndrome (PMS) symptoms when compared to a placebo (26).

In light of the negative effect that premenstrual syndrome (PMS) has on women's personal and professional lives, as well as the significant rate of discontinuation of conventional drugs, alternative therapy modalities are warranted. However, the existing research on HypericumPerforatum is limited and has yielded inconsistent findings. Therefore, further investigations are warranted to explore the effect of this botanical species on premenstrual syndrome (PMS). Hence, the objective of this research was to examine the effect of HypericumPerforatum on the severity of premenstrual syndrome (PMS) symptoms.

**Method**

The presentstudy was conducted as a double-blind clinical trial, incorporating a control group. The research study encompassed the entire statistical population of women between the ages of 18 and 35 who were diagnosed with premenstrual syndrome and sought treatment at Isar Rehabilitation Clinic. From this population, a sample of 105 participants was chosen using convenience sampling, and these individuals were then randomly assigned to two separate groups. The inclusion criteria for this study

encompassed individuals who exhibited regular menstruation cycles lasting between 24 and 35 days. Additionally, participants were required to be free from mental illness, and physical ailments such as seizures, heart diseases, obesity, and thyroid disorders. They were also excluded if they were presently taking hormonal drugs, anticoagulants, antidepressants, supplements, or herbal medicines. Furthermore, individuals who were undergoing treatment for premenstrual syndrome, consuming alcohol or drugs, sensitive to sunlight, experiencing recent bereavement within the past three months, had undergone surgery within the past three months, or had been diagnosed with other depressive disorders as per the DSM-5 were not eligible for inclusion in the study. The exclusion criteria encompassed several factors, including participants who expressed a lack of willingness to continue their involvement in the study, individuals who experienced side effects or showed sensitivity to the medicine, participants who chose to discontinue their prescription, and individuals who through significant life events such as marriage, the loss of immediate family members, or pregnancy throughout the study. According to Khademi's (2020) research, the study employed a sample size of 50 individuals for each group (24). To address the issue of non-participation and non-compliance with the inclusion and exclusion criteria, a total of 120 individuals were chosen for the study. Ultimately, the data of 105 participants, divided into the placebo group (n=52) and the perforan group (n=53), were analyzed. The specific findings are presented in Figure 1. During the pre-test stage, also known as Cycle 1, women who were selected for the study underwent the administration of the Premenstrual Symptoms Screening Questionnaire (PSST). The participants were administered perforan and placebo pills in a standardized and coded manner by a midwife who was blinded to the groups and codes. Additionally, the participants were provided with instructions regarding the dosage and administration of the medications. During the second cycle, also known as the post-test phase, the participants were once again required to complete the PSST. This process was repeated in the third cycle or follow-up.

**Data Collection Instrument**

**Premenstrual Symptoms Screening Questionnaire (PSST)**

The questionnaire in question was developed by Steiner et al. (2003) (27). The present investigation employed the Persian version of the PSST, as standardized by Siahbazi et al. (28). The present questionnaire has a total of 19 inquiries and serves the objective of assessing the symptoms associated with premenstrual syndrome. Each question inquires about four criteria, namely: not at all, mild, moderate, and severe. These criteria are assigned numerical values ranging from 0 to 3. The questionnaire consists of two sections. The first section encompasses 14 symptoms related to emotional, physical, and behavioral symptoms. The mentioned symptoms are anger (irritability), anxiety (tension), crying (increased sensitivity to negative response), depressed mood (despair), decreased interest in work activities, decreased interest in household activities, decreased interest in activities social, difficulty concentrating, fatigue (lack of energy), overeating (cravings), insomnia, hypersomnia (needing more sleep), feeling agitated or out of control, and physical symptoms (breast pain, headache, muscle/joint pain, abdominal bloating, weight gain). The second section comprises a set of five inquiries about the effect of these symptoms on the overall quality of life. Female participants were inquired about the extent to which their aforementioned symptoms impede their functioning in five distinct domains: job performance, interpersonal interactions with colleagues and acquaintances, familial relationships, engagement in social activities, and fulfillment of family responsibilities. The criteria delineated in this questionnaire align with the diagnostic criteria for premenstrual dysphoric disorder (PMDD) as outlined in the DSM-IV and DSM-V (29, 30).

To establish a diagnosis of moderate or severe premenstrual syndrome (PMS), the following three criteria must be conpresently met: from the available items numbered 1 to 4, at least one must be moderate or severe. In conjunction with the aforementioned item, it is imperative that, within the range of items 1 to 14, at least four items must be moderate or severe. In case of the effect of symptoms on life (five last items), moderate or severe items must be available. The reliability test of this tool conducted in Iran yielded a Cronbach's alpha coefficient of 0.9 (28).

**Interventions**

**HypericumPerforatum**

The participants in the study were administered perforan tablets, which were manufactured by Goldaru business and had the product code PG115014. During the initial cycle, for one month, the participants were administered perforan capsules at a daily dosage of 280 mg. In the succeeding cycles, the participants were administered perforan capsules starting from 8 days before the onset of menstruation and continuing until 2 days after menstruation. (24)

**Placebo**

The participants were administered a capsule containing oral paraffin, which closely resembled Perforan.

**Data Analysis**

To conduct data analysis, various descriptive statistics were employed, including mean and standard deviation. Additionally, inferential statistics, such as the Mann-Whitney U test, Chi-square test, and analysis of variance with repeated

measures, were utilized. The data analysis was conducted utilizing SPSS 26.

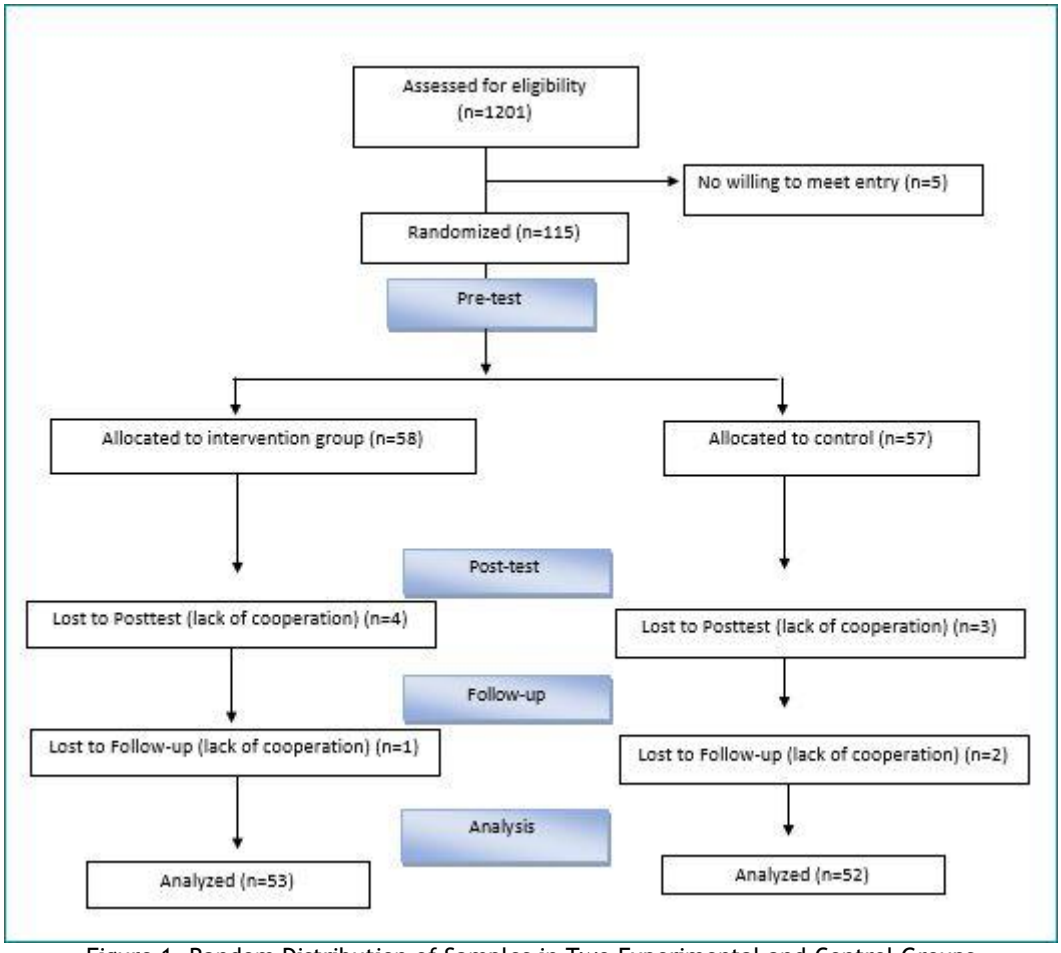


Figure 1. Random Distribution of Samples in Two Experimental and Control Groups

**Results**

The findings of the present study indicate that there were no significant differences between the experimental and control groups in terms of demographic factors, including age, menstrual cycle length, BMI, education level, menarche age, and duration of menstrual bleeding. These related data are presented in Tables 1 and 2.

The results of the present study show that the mean (standard deviation) of the placebo and perforan groups in the pre-test is 33.51 (9.61), and 34.47 (10.26) respectively). In the post-test, it is 30.15 (12.37), 24.47 (13.06), and in the follow-up, it is 28.57 (12.01), 22.26 (12.39), which is shown in Table 3.

Table 4 shows that there is a homogenous correlation between the variables under study. The assumption of homogeneity of the covariance matrix has been met because the observed F related to this test is not statistically significant at the $p<0.05$ level. Because the observed F associated with this test in the researched variables is not statistically significant at the $p<0.05$ level, Table 5 demonstrates that the error variance is homogeneous in the studied groups and that the assumption of homogeneity of error variance has also been met. Table 6 shows that the equality of covariance assumption has been rejected ($P<0.05$).

The data analysis for this research was conducted using repeated measure variance analysis. Among the main assumptions of this analysis, only two assumptions (Mbox and Lone) were met, while Mauchly's test of sphericity was not met. To address this issue and test the hypothesis of the research, the Greenhouse-Geisser test was employed. The results of this test are presented in Table 7. Based on the findings from many iterations of analysis of variance, it can be concluded that there is a substantial effect of time ($P<0.05$, $F=29.189$) on the intensity scores of premenstrual syndrome symptoms. Furthermore, the interaction effect between groups and time is also found to be significant ($P<0.05$, $F=5.825$). The findings of this study suggest that there are variations in the levels of PMS symptom severity scores across multiple time points, including pre-test, post-test, and follow-up.

The LSD test was employed to detect and analyze these alterations, as outlined in Table 8 and Figure 2. The findings indicate a statistically significant difference in PSST scores among pre-test, post-test, and follow-up assessments (P<0.05). However, there was no statistically significant difference between post-test and follow-up scores. Additionally, the results suggest that the administration of Perforan has led to a notable decrease in the severity of premenstrual syndrome (PMS) symptoms among the participants in the experimental group when compared to those in the control group (F=4.041, P<0.05). This can be observed in Table 9 and Figure 3. Furthermore, the analysis revealed a significant interaction effect between the group and time variables, indicating that the therapeutic regimen had a notable effect on reducing PMS symptom scores in the experimental group when compared to the control group. This effect was observed in both the post-test and follow-up assessments, as compared to the pre-test evaluation (F=5.825, P<0.05). The related data are depicted in Figure 4.

Table 1. Independent t-test Results for Demographic Findings

| | Menstrual Cycle (Days) | BMI | Age | Age At Menarche | Duration Of Menstrual Bleeding |
|---|---|---|---|---|---|
| Mann-Whitney U | 1368.500 | 1195.500 | 1238.000 | 1308.000 | 1370.000 |
| Wilcoxon W | 2799.500 | 2573.500 | 2669.000 | 2739.000 | 2801.000 |
| Z | -.066 | -1.170 | -.900 | -.471 | -.053 |
| Asymp. Sig. (2-tailed) | .947 | .242 | .368 | .638 | .958 |

Table 2. Chi-square Test Results for Demographic Findings

| Group | | | | Chi-square | p |
|---|---|---|---|---|---|
| | | Placebo | Perforan | | |
| education | Under high school diploma | 2 | 2 | 7.350 | 0.19 |
| | Diploma | 7 | 13 | | |
| | Associate degree | 4 | 4 | | |
| | BA | 28 | 16 | | |
| | MA | 11 | 17 | | |
| | Phd | 0 | 1 | | |
| Total | | 52 | 53 | | |

Table3. Descriptive Statics

| | Group | Mean | Std. Deviation | N |
|---|---|---|---|---|
| Pretest | placebo | 33.5192 | 9.61512 | 52 |
| | Perforan | 34.4717 | 10.26870 | 53 |
| Posttest | placebo | 30.1538 | 12.37230 | 52 |
| | Perforan | 24.4717 | 13.06876 | 53 |
| Follow-up | placebo | 28.5769 | 12.01200 | 52 |
| | Perforan | 22.2642 | 12.39440 | 53 |

Table 4. The Results of M. Box test

| | |
|---|---|
| Box's M | 9.036 |
| F | 1.458 |
| df1 | 6 |
| df2 | 76787.626 |
| Sig. | .188 |

Table5: Levene's Test of Equality of Error Variances

| | | Levene Statistic | df1 | df2 | Sig. |
|---|---|---|---|---|---|
| Pretest | Based on Mean | .147 | 1 | 103 | .702 |
| Posttest | Based on Mean | .197 | 1 | 103 | .658 |
| Follow-up | Based on Mean | .012 | 1 | 103 | .914 |

Table6. Mauchly's Test of Sphericity

| Within Subjects Effect | Mauchly's W | Approx. Chi-Square | df | Sig. | Epsilon | | |
|---|---|---|---|---|---|---|---|
| | | | | | Greenhouse-Geisser | Huynh-Feldt | Lower-bound |
| time | .867 | 14.506 | 2 | .001 | .883 | .906 | .500 |

Table7: Tests of Within-Subjects Effects

| Source | Type III Sum of Squares | df | Mean Square | F | Sig. | Partial Eta Squared |
|---|---|---|---|---|---|---|
| Time | 4261.504 | 1.766 | 2413.217 | 29.189 | .000 | .221 |
| time * group | 850.419 | 1.766 | 481.578 | 5.825 | .005 | .054 |
| Error(time) | 15037.670 | 181.888 | 82.676 | | | |

Table8. Pairwise Comparisons

| (I) time | (J) time | Mean Difference (I-J) | Std. Error | Sig. | 95% Confidence Interval for Difference | |
|---|---|---|---|---|---|---|
| | | | | | Lower Bound | Upper Bound |
| Pretest | Posttest | 6.683* | 1.134 | .000 | 4.433 | 8.932 |
| | Follow-up | 8.575* | 1.368 | .000 | 5.862 | 11.288 |
| Posttest | Pretest | -6.683* | 1.134 | .000 | -8.932 | -4.433 |
| | Follow-up | 1.892 | 1.007 | .063 | -.104 | 3.889 |
| Follow-up | Pretest | -8.575* | 1.368 | .000 | -11.288 | -5.862 |
| | Posttest | -1.892 | 1.007 | .063 | -3.889 | .104 |

*The mean difference is significant at the .05 level

Table 9: Tests of Between-Subjects Effects

| Source | Type III Sum of Squares | df | Mean Square | F | Sig. | Partial Eta Squared |
|---|---|---|---|---|---|---|
| Intercept | 263241.927 | 1 | 263241.927 | 997.001 | .000 | .906 |
| group | 1066.841 | 1 | 1066.841 | 4.041 | .047 | .038 |
| Error | 27195.489 | 103 | 264.034 | | | |

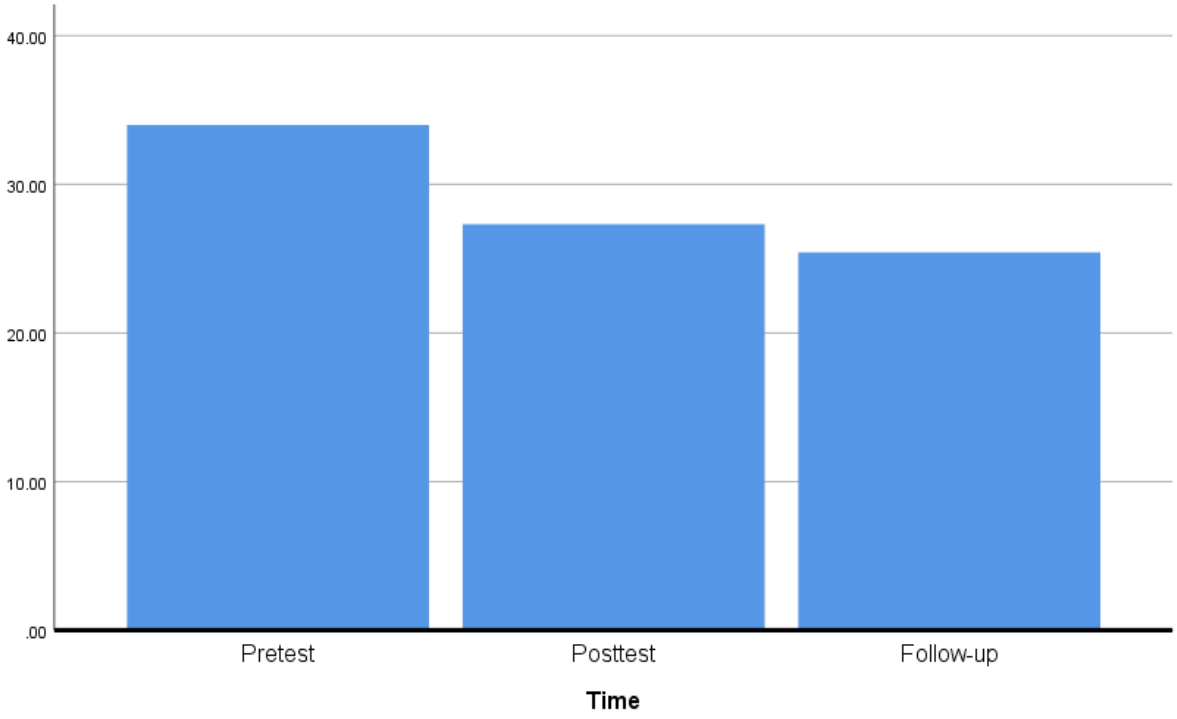


Figure 2. The Effect of Perforan on Reducing PMS Symptoms in Pre-test, Post-test and Follow-up

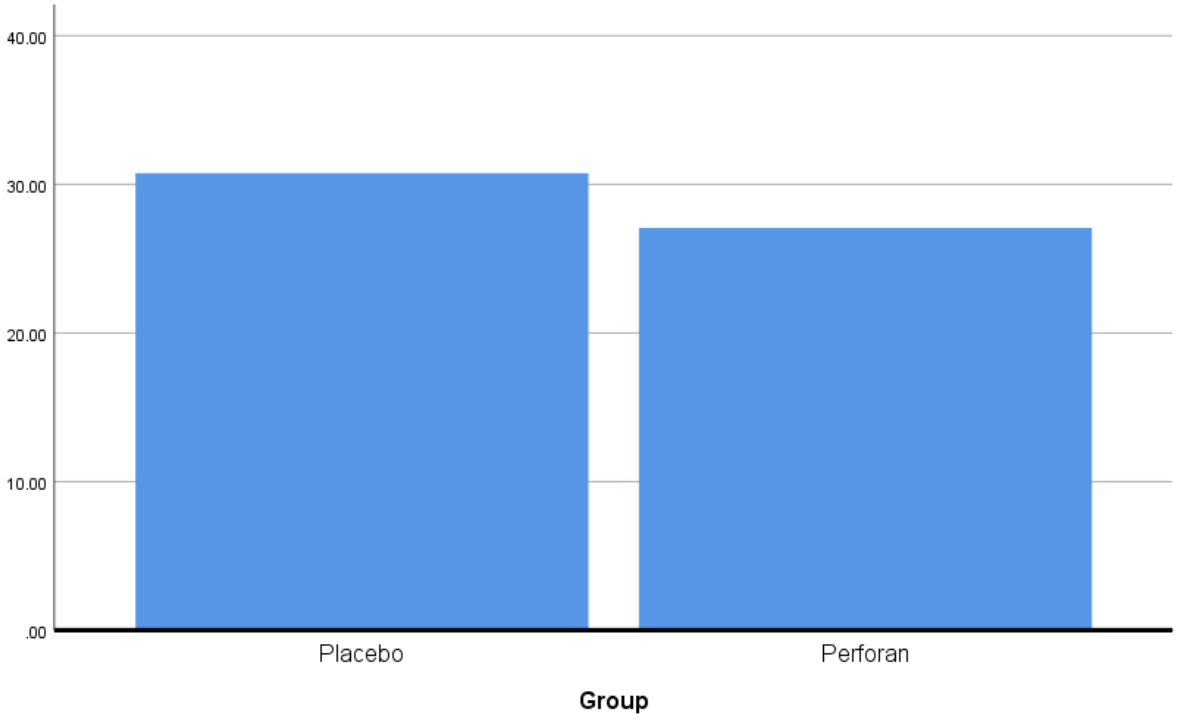


Figure 3. The Effect of Perforan on Reducing PMS Symptoms in both Experimental and Control Groups

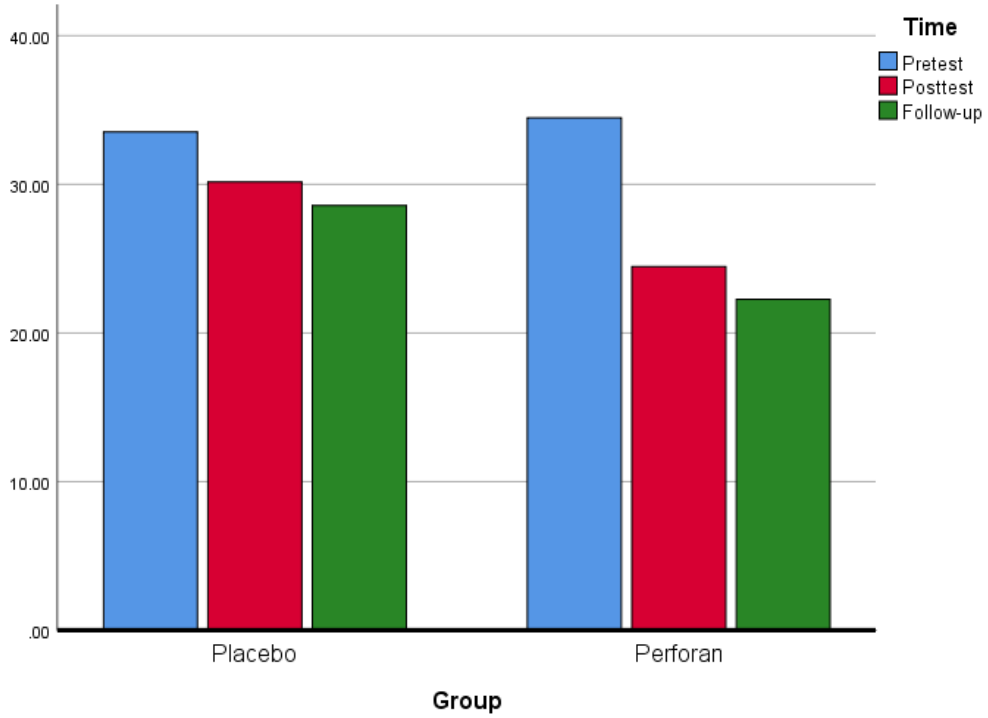


Figure 4. Interactive Effect of Group and Time on Symptom Severity Scores

**Discussion**

The results of the present study indicate that Perforan exhibits a statistically significant reduction in premenstrual syndrome (PMS) symptoms when compared to a placebo. The aforementioned discovery suggests that the ingestion of Perforan exhibits efficacy in mitigating symptoms associated with premenstrual syndrome during the post-test and follow-up periods. The study conducted by Khademi et al. (2020) demonstrated that the administration of Perforan resulted in a considerable reduction in the intensity of both physical and behavioral symptoms associated with premenstrual syndrome (PMS) (24). In a separate study examining the efficacy of HypericumPerforatum, Vitexagnus, and vitamin E as therapies for premenstrual syndrome (PMS), it was demonstrated that all three interventions effectively mitigate the intensity of PMS symptoms (25). In a study conducted by Sabet-Birjandi et al. (2011), a comparison was made between perforan and vitamin B6 in terms of their efficacy in alleviating psychological symptoms associated with premenstrual syndrome (PMS). The findings of the study indicated that only perforan showed a significant reduction in these symptoms. Vitamin B6 has been found to effectively alleviate both physical and psychological problems, as indicated by previous research (31). Canning et al. (2010) conducted a study that yielded contrasting findings compared to the study conducted by Sabet-Birjandi et al. The study found that there was no significant difference between the improvement of mood-related symptoms and pain in the treatment group compared to the placebo group (23). In the present investigation, the lack of independent examination of premenstrual syndrome (PMS) symptoms and the sole comparison of the overall score of the scale have resulted in an unclear alignment with any specific study. Pakgohar et al. (2005) conducted a study that showed that the use of 60 drops of Hyperion, a supplement containing HypericumPerforatum, daily for two months during the luteal phase, resulted in a significant reduction in premenstrual syndrome symptoms (22).

The findings suggest that the antioxidant properties of perforan, derived from the flavonoids and folic acids present in HypericumPerforatum, along with its ability to inhibit the reabsorption of serotonin, norepinephrine, γ-aminobutyric acid (GABA), L-glutamate, and dopamine through hypericin and hyperforin, contribute to its potential in reducing symptoms of premenstrual syndrome (PMS) (19, 18, 20, 21).

Furthermore, a study conducted by Hicks et al. (2004) demonstrated that there is no statistically significant distinction observed between the intervention and placebo cohorts in terms of mitigating menstruation symptoms and alleviating premenstrual syndrome (PMS) symptoms (26). When elucidating this discovery, one can attribute it to variations in pharmaceutical dosage, the period of pharmaceutical administration, and the metric employed for measurement. However, Hicks et al. (2004) have admitted that the absence of statistical significance in their investigation may not be attributed to St. John's wort extract, but rather to inadequate statistical power (26).

The main limitation of the present study lies in the utilization of a convenience sampling method, hence warranting the recommendation for future

research endeavors to employ a random sample method. Furthermore, as a result of time limitations, the feasibility of conducting long-term follow-ups was limited. Therefore, it is recommended that future studies incorporate 3-month and 6-month follow-up assessments.

**Conclusion**

The results of the present study indicate that Perforan demonstrates efficacy in mitigating symptoms associated with premenstrual syndrome (PMS). Hypericumperforatum, often known as St. John's Wort, has demonstrated efficacy in alleviating symptoms of premenstrual syndrome (PMS) in women. Notably, this herbal remedy exhibits a favorable side effect profile compared to conventional treatments like selective serotonin reuptake inhibitors (SSRIs) and tricyclic medications. Nevertheless, there is a scarcity of research undertaken in this particular domain. Hence, it is imperative to undertake additional clinical trials to examine the effect of HypericumPerforatum.

**references**


1. Odongo E, Byamugisha J, Ajeani J, Mukisa J. Prevalence and effects of menstrual disorders on quality of life of female undergraduate students in Makerere University College of health sciences, a cross sectional survey. BMC Women's Health. 2023;23(1):1-9.
2. Shi Y, Shi M, Liu C, Sui L, Zhao Y, Fan X. Associations with physical activity, sedentary behavior, and premenstrual syndrome among Chinese female college students. BMC Women's Health. 2023;23(1):1-9.
3. Ryu A, Kim T-H. Premenstrual syndrome: A mini review. Maturitas. 2015;82(4):436-40.
4. Chen Z, Imai K, Zhou X. The relationship between physical activity and premenstrual syndrome in senior high school students: a prospective study. Scientific Reports. 2023;13(1):5881.
5. Upadhyay M, Mahishale A, Kari A. Prevalence of premenstrual syndrome in college going girls-A cross sectional study. Clinical Epidemiology and Global Health. 2023;20:101234.
6. Babapour F, Elyasi F, Shahhosseini Z, Hosseini Tabaghdehi M. The prevalence of moderate–severe premenstrual syndrome and premenstrual dysphoric disorder and the related factors in high school students: A cross-sectional study. Neuropsychopharmacology Reports. 2023.
7. Bhandari S, Dwa Y, Maharjan M, Maskey S, Thakur M, Sharma S. Premenstrual Syndrome among Medical Students of a Medical college: A Descriptive Cross-sectional Study. JNMA: Journal of the Nepal Medical Association. 2023;61(260):347.
8. AbdelQadir YH, Assar A, Abdelghafar YA, Kamal MA, Zaazouee MS, Elsayed SM, et al. Prevalence and patterns of premenstrual disorders and possible association with sexual harassment: a cross-sectional study of young Arab women. BMC women's health. 2022;22(1):1-10.
9. Eshetu N, Abebe H, Fikadu E, Getaye S, Jemal S, Geze S, et al. Premenstrual syndrome, coping mechanisms and associated factors among Wolkite university female regular students, Ethiopia, 2021. BMC Women's Health. 2022;22(1):88.
10. Alkhatib A, Zhou Q, Bajinka O, Pakwan Suwal R, Wiley J, Li X. Prevalence of menstrual symptoms change and influencing factors among international female students studying in china during acculturation period. BMC Women's Health. 2022;22(1):1-11.
11. Connolly M. Premenstrual syndrome: an update on definitions, diagnosis and management. Advances in psychiatric treatment. 2001;7(6):469-77.
12. Hashemi S, Tehrani FR, Mohammadi N, Dovom MR, Torkestani F, Simbar M, et al. Comparison of metabolic and hormonal profiles of women with and without premenstrual syndrome: A community based cross-sectional study. International journal of endocrinology and metabolism. 2016;14(2).
13. Dimmock PW, Wyatt KM, Jones PW, O'Brien PS. Efficacy of selective serotonin-reuptake inhibitors in premenstrual syndrome: a systematic review. The lancet. 2000;356(9236):1131-6.
14. Hantsoo L, Epperson CN. Allopregnanolone in premenstrual dysphoric disorder (PMDD): Evidence for dysregulated sensitivity to GABA-A receptor modulating neuroactive steroids across the menstrual cycle. Neurobiology of Stress. 2020;12:100213.
15. Jahanfar S, Lye M-S, Krishnarajah IS. The heritability of premenstrual syndrome. Twin Research and Human Genetics. 2011;14(5):433-6.
16. Harlow SD, Campbell OM. Epidemiology of menstrual disorders in developing countries: a systematic review. 2004.
17. Naghdi Badi H, Amin G, Makkizadeh M, Ziai S. St. John's wort (Hypericum perforatum L.): A Review. Journal of Medicinal Plants. 2005;4(16):1-14.
18. Barnes J, Anderson LA, Phillipson JD. St John's wort (Hypericum perforatum L.): a review of its chemistry, pharmacology and clinical properties. Journal of pharmacy and pharmacology. 2001;53(5):583-600.
19. Orčić DZ, Mimica-Dukić NM, Francišković MM, Petrović SS, Jovin EĐ. Antioxidant activity relationship of phenolic

compounds in Hypericum perforatum L. Chemistry Central Journal. 2011;5:1-8.
20. Zanoli P. Role of hyperforin in the pharmacological activities of St. John's Wort. CNS drug reviews. 2004;10(3):203-18.
21. Kholghi G, Arjmandi-Rad S, Zarrindast M-R, Vaseghi S. St. John's wort (Hypericum perforatum) and depression: what happens to the neurotransmitter systems? Naunyn-Schmiedeberg's Archives of Pharmacology. 2022;395(6):629-42.
22. Pakgohar M, Ahmadi M, Salehi surmaghi M, Mehran A, Akhondzadeh S. Effect of Hypericum perforatum L. for treatment of premenstrual syndrome. Journal of Medicinal Plants. 2005;4(15):33-42.
23. Canning S, Waterman M, Orsi N, Ayres J, Simpson N, Dye L. The efficacy of Hypericum perforatum (St John's wort) for the treatment of premenstrual syndrome: a randomized, double-blind, placebo-controlled trial. CNS drugs. 2010;24:207-25.
24. Khademi N, Abbassinya H, Heshmat F, Naafe M, Mohammadbeigi A. Evaluation of the effect of perforan (Hypericum perforatum) on premenstrual syndrome severity of physical and behavioural symptoms in patients with premenstrual syndrome: A clinical randomised trial. Advances in Human Biology. 2020;10(3):110-4.
25. Salehi A, Momeni H, Seraji A. Comparison of the effects of Hypericum and Vitex agnus premenstrual syndrome compared with vitamin E: a randomized clinical trial. complementary Medicine Journal. 2013;3(1):395-405.
26. Hicks SM, Walker AF, Gallagher J, Middleton RW, Wright J. The significance of" nonsignificance" in randomized controlled studies: a discussion inspired by a double-blinded study on St. John's wort (Hypericum perforatum L.) for premenstrual symptoms. Journal of Alternative & Complementary Medicine. 2004;10(6):925-32.
27. Steiner M, Macdougall M, Brown E. The premenstrual symptoms screening tool (PSST) for clinicians. Archives of Women's Mental Health. 2003;6:203-9.
28. Siahbazi S, Hariri FZ, Montazeri A, Banaem LM. Translation and psychometric properties of the Iranian version of the Premenstrual Symptoms Screening Tool (PSST). Payesh (Health Monitor). 2011;10(4):421-7.
29. Rapkin AJ, Korotkaya Y, Taylor KC. Contraception counseling for women with premenstrual dysphoric disorder (PMDD): current perspectives. Open Access Journal of Contraception. 2019:27-39.
30. Jafari F, Tabarrai M, Abbassian A, Jafari F, Ayati MH. Effect of garlic (Allium sativum) supplementation on premenstrual disorders: A randomized, double-blind, placebo-controlled trial. Evidence-Based Complementary and Alternative Medicine. 2021;2021.
31. sabet-birjandi S, Tadayon-Najafabadi M, Siyahpooshan A, Haghighizadeh MH. Comparision the effect of Hypericum perforatum and vitamin B6 in the treatment of premenstrual syndrome. Zahedan J Res Med Sci. 2011;13(4):e93929.