

## Use of Medicinal Plants in the Treatment of Premenstrual Syndrome: A Review

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**Abstract:** Premenstrual syndrome is a common condition in women and includes a range of emotional, psychological, and physical symptoms triggered by the menstrual cycle. Complementary and alternative medicine use is more prevalent in the treatment of diseases, and many women use medicinal plants without a physician's prescription. Modified diet and use of herbal medicine may be one effective method in the treatment of premenstrual syndrome. The purpose of this study was to collect information about medicinal plants used in the treatment of premenstrual syndrome. This review studied articles obtained from data bases, *Pubmed*, *Science Direct*, *MD Consult*, *Inter Science*, and *Iran Medex* from 2000-2010. Several studies and trials have shown a reduction of premenstrual syndrome symptoms after consumption of *Hypericum perforatum*, *Vitex agnus castus*, saffron, ginkgo, and soy rather than the placebo group. Medicinal plants can be used in the treatment of premenstrual syndrome if certain precautions are followed. More studies are needed about these and other plants.

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### 1. Introduction

Premenstrual syndrome (PMS) is a common condition (Jurgens, 2009; Canning, 2010) and a collection of symptoms, ranging from physical to behavioral, which begin one to two weeks prior to menstruation and diminish with the onset of menstruation (Jurgens, 2009). Symptoms can be severe enough to overshadow family activities, and interfere with social or professional obligations of the affected individual (Kimural, 2007; Adriane, 2000). PMS has been reported to occur in at least 75 percent of women at some point during their reproductive years (Jurgens, 2009). About 30-80 percent of women have mild to moderate symptoms of PMS in each cycle, but only 2.5 percent of women exhibit symptoms so severe that they interfere in everyday activities (Bryant, 2005; Clare, 2001). Although there is a wide range of symptoms, the primary cause is unknown probably the result of several factors (Jurgens, 2009). There are several potential hormonal scenarios involved in the etiology of PMS: estrogen dominance, progesterone dominance, too much prolactin, vitamin/mineral deficiencies, reduce indorphin, disorder prostaglandin metabolism, low levels of serotonin, and psychological factors (Canning, 2010; Ryan, 2008, Marsden, 2003; Berek, 2003). Also, there are factors like hormonal imbalance, reduced progesterone-to-estrogen ratio, sodium retention, lack of nutrients such as Vit. B6, Mg, Ca, inappropriate response to neurotransmitters, abnormal function axis hypothalamus - pituitary - adrenal defect that leads to adrenal hormone secretion

and environmental factors such as stress (Braverman, 2007; Clare, 2001).

The most common age is for symptoms to appear is between 25 to 45 years. PMS symptoms are quite variable. The most common symptoms are: abdominal pain, mood instability, irritability, nervous tension, headache, increased appetite, palpitations, weakness, dizziness and fainting, weight gain, swollen hands and feet, swelling and sensitivity of breast, penchant to sweets, feel of swelling and abdominal bloating, depression, poor memory, and insomnia (Clare and Subhash, 2001).

Many treatment approaches have used a range of western drugs and non-drug therapies with varying outcomes (Morse, 2007). Drug treatments include antidepressants, diuretics, progesterone, estrogen replacement, pyridoxine and GnRH agonists and supplement treatment. Chemical drugs used to treat PMS have many side effects, including gastrointestinal disorders, kidney failure, etc. (Kimural, 2007; Schellenberg 2001). Most women do not require long-term drug treatment and medication is not needed for moderate symptoms. Nutritional therapies are popular, but lack a clear evidence base. Although there is little research to determine the effects of alternative medicines, many women are using them (Canning, 2006). As many as 80 percent of women suffering from symptoms of PMS report self-medicating with over-the-counter (OTC) products, including natural health products (NHPs) such as herbs, vitamins, and minerals (Jurgens and Whelan, 2009). As women search for ways to treat the troublesome symptoms of premenstrual syndrome

(PMS), many hope to find a natural option (Marsden, 2003). Since PMS is a chronic condition, we must note side effects of medications. Herbal medicine has recently been recognized as acceptable treatment because it has fewer side effects (Ozgoali, 2009). One study found that the most common treatment in Asian women was hormones (32 percent) while in European group, phytotherapy/vitamins prevailed (48 percent) (Facchinetti, 2007). The purpose of this study to collect information about medicinal plants used in the treatment of premenstrual syndrome.

This review studied data obtained from *Pubmed*, *Science Direct*, *MD Consult*, *Inter Science*, and *Iran Medex* databases between 2000-2010. Key search terms were: complementary medicine, alternative therapy, premenstrual syndrome, PMS. The results of studies have been resulted such as clinical trial, case-control studies.

## 2. Discussions

### 2.1 Chasteberry (*Vitex agnus castus*)

Chasteberry (*Vitex agnus-castus*), or monk's pepper, is found in western Asia, southwestern Europe, and much of the southeastern United States (Roemheld-Hamm, 2005). Chasteberry has been used for several centuries in the treatment of hormone-dependent gynecologic diseases. Recent studies support its use for periodic breast discomfort related to premenstrual syndrome (Roemheld-Hamm, 2005; Gorkow, 2002). The main mechanism is not known but it impacts dopamine receptors and reduces the secretion of prolactin. It is assumed that vitex stimulates the release of luteinizing hormone (LH) that leads to release of progesterone. Increased progesterone reduces the secretion of estrogen. Its indirect and direct effect on progesterone and prolactin result in an improved balance in the luteal phase of the menstrual cycle (Stevinson, 2000).

Chasteberry is well-tolerated. Its few reported side effects may include gastrointestinal discomfort, dizziness, and dry mouth. Drug interactions have not been reported, but caution is recommended for its use with dopamine agonists or antagonists (Roemheld-Hamm, 2005). Randomized controlled trials showed that chasteberry is helpful in reducing symptoms of PMS/PMDD such as irritability, mood, anger, breast fullness and tenderness, headache, cramps, water retention, swelling, and food cravings (Jurgens, 2009).

A 2001 BMJ study evaluated 170 women with PMS symptoms. Women were randomized and blinded for receiving either vitex or placebo. Participants were evaluated for irritability, mood alteration, anger, headache, and breast tenderness and bloating. After three consecutive menstrual cycles, 52 percent of the vitex group had a 50 percent or greater decrease in symptoms versus only 24 percent of

placebo patients. Vitex relieved irritability, mood swings, anger, and headache and breast tenderness but not bloating (Marsden, 2003).

A study by Aqajani and colleagues was performed in Babol University of Medical Sciences to evaluate *vitex agnus castus* in PMS treatment. This study was performed on 20 patients with PMS. Diagnosis of PMS was conducted through interviews according to COPE (Calendar of Premenstrual Experiences). The severity of symptoms was given a score zero (absence of symptoms) to three (severe symptoms prohibiting activity). Patients in both groups (10 people per group) received *vitex agnus castus* and placebo drops. Both groups used 30 drops of the drug twice a day for at least five days before menstruation for three consecutive cycles. After three months of treatment, researchers recorded physical and psychological symptoms through questionnaires and interviews. At the end of research, they showed 70 percent improvement in the treated group with *vitex agnus castus* and 30 percent improvement in the placebo group. Therefore they recommended that women with PMS receive medical *vitex agnus castus* (Aqajani, 2002).

A double-blind clinical trial was conducted to assess *agnus castus* in the treatment of premenstrual syndrome in Germany. In this study, 170 women in the control group (84 cases) and intervention group (86 cases) were sampled. The mean age was 36 years and the average menstrual cycles was 28 days. Both of groups received a drug (*agnus castus* or placebo) - one tablet daily for three months. At the end of the study, there was a 52 percent improvement in the *agnus castus* group and 24 percent in the placebo group, a significant difference between two groups (Schellenberg, 2001). A prospective randomized double-blind placebo-controlled study was conducted to assess the efficacy of the extract of *vitex agnus castus* (VAC) in the treatment of 67 Chinese women with moderate to severe premenstrual syndrome (PMS). Women received one tablet of VAC or placebo. Researchers documented symptoms with a daily rating scale with negative effect, water retention, food cravings, and pain. The result was that all four symptom factor scores were significantly reduced by the third treatment cycle. They concluded that *vitex agnus castus* extract was effective in treating moderate to severe PMS in Chinese women, especially in symptoms of negative affect and water retention (Ma, 2010). Atmaca et al. compared the efficacy of fluoxetine with *vitex agnus castus* extract and concluded that fluoxetine was more effective for psychological symptoms although the extract decreased the physical symptoms (Atmaca, 2003).

Adverse effects of *vitex agnus castus* include GI upset, nausea, vomiting, headache, rash, acne, and irregular menstrual cycle. Researchers used a different preparation of chasteberry, ranging from a crude extract of *vitex agnus castus* (20–40 mg/day) to 20 mg/day of an extract (fruit extract ZE 440:60 percent ethanol 6-12:1) standardized to casticin. Drug interactions were theoretical, but documentation was lacking (Jurgens, 2009).

Several different studies have shown that products containing *vitex agnus castus* fruit extract are useful for decreasing prolactin serum levels and increasing pathophysiological and can be a good treatment for women who suffer from premenstrual syndrome (Doll, 2009). A study showed that *vitex agnus castus* is a safe, well-tolerated, and useful drug for the treatment of moderate to severe PMS (He, 2009).

## 2.2 *Hypericum perforatum* (St. John's wort)

*Hypericum perforatum* (St. John's wort) is a medicinal plant that prompts amino-oxidase activity and prevents serotonin reuptake. It reduces premenstrual syndrome symptoms with treatment properties similar to fluoxetine. Several studies have shown that it is effective in the treatment of mild types of depression. For the treatment of premenstrual symptoms its use is for at least two months in the luteal phase (Pakghohar, 2005). If this plant is used in high doses, it can cause sensitivity to light (Van, 2009). Adverse effects include GI upset, nausea, diarrhea, insomnia, irritability, agitation, forgetfulness, dizziness, headache, dry mouth, worsening of PMS symptoms, bloating, breast tenderness, and rashes (Jurgens, 2009). Its drug interactions are anesthetics, anticoagulants/antiplatelets, antidepressants, antidiabetic agents, barbiturates, benzodiazepines, beta-adrenergic blockers, calcium channel blockers, cyclosporine, HIV protease inhibitors, etc. (Jurgens, 2009; Van, 2009).

Canning et al. (2010) investigated the effectiveness of *hypericum perforatum* on symptoms of PMS in UK. They conducted a randomized, double-blind, placebo-controlled, crossover study between November 2005 and June 2007. In this study, 36 women, who remained eligible after three screening cycles, underwent a two-cycle placebo run-in phase. They randomly received *hypericum perforatum* tablets 900 mg/day (standardized to 0.18 percent hypericin; 3.38 percent hyperforin) or placebo tablets for two menstrual cycles. After a placebo-treated period, the women crossed over to receiving placebo or *hypericum perforatum* for two additional periods. Symptoms were recorded daily using the Daily Symptom Report. The results

indicated that the effect of *hypericum perforatum* was statistically better than the placebo in improving physical and behavioral symptoms of PMS. A significant difference in the treatment of pain-related PMS symptoms was not found. They concluded that treatment with *hypericum perforatum* was more effective than placebo for the most common physical and behavioral symptoms associated with PMS (Canning, 2010).

Pakghohar and colleagues did a double-blind clinical trial on 70 students with PMS at Tehran University in 2005. After confirmation of PMS symptoms by the completion of daily symptoms for two consecutive cycles, participants were randomly divided into two groups. Samples were treated with 30 drops of *hypericum perforatum* (happyran) and placebo twice a day at least seven days before menstruation for a duration two consecutive cycles. PMS symptoms decreased after consumption of *hypericum perforatum* 46.45 percent and in the placebo group 18.1 percent. They concluded that treatment of PMS with happyran is effective (Pakghohar, 2005).

A pilot study was performed at Exeter University. In their study, 19 women with PMS were treated with 300 mg standard happyrysyn 3 percent. The results showed a 51 percent reduction in PMS score and at least a 50 percent reduction in symptoms for more than two thirds of women (Stevinson, 2000). A study showed the herbal combination of *hypericum perforatum* and *vitex agnus castus* to be superior to the placebo for total PMS-like scores, PMS-D, and PMS-C clusters. Also it was shown to reduce anxiety and hydration clusters in the treated group (Van, 2009).

## 2.3 Saffron (*crocus sativus*)

Saffron was effective in relieving overall symptoms of PMS in one good-quality randomized control trials. Adverse effects of saffron were increased or decreased in appetite, headache, hypomania, sedation, and nausea. Saffron poisoning was reported at high doses (5 g). Drug interactions were not reported (Jurgens, 2009). Agha-Hosseini et al. (2008) conducted a double-blind and placebo-controlled trial to investigate whether saffron (stigma of *crocus sativus* L.) could relieve symptoms of premenstrual syndrome (PMS) in Tehran and Zanjan. Women who were 20 to 45 years old and had regular menstrual cycles and PMS symptoms for at least six months were selected for the study. Women were randomly divided into two groups and received capsule saffron 30 mg/day (15 mg twice a day - morning and evening) (group A) or capsule placebo (twice a day) for two menstrual cycles (cycles three and four).

Researchers found that saffron was effective in relieving symptoms of PMS. It was shown that saffron was significantly effective in cycles three and four in the total Premenstrual Daily Symptoms and Hamilton Depression Rating Scale. They concluded that *crocus sativus L.* can be used in the treatment of PMS. However, further investigation is needed (Agha-Hosseini, 2008).

## 2.4 Ginkgo biloba L.

Ginkgo biloba is used in traditional Chinese medicine. Clinical studies have shown that ginkgo extracts have a therapeutic effect in Alzheimer's disease, failing memory, age-related dementias, poor cerebral and ocular blood flow, congestive symptoms of premenstrual syndrome, and the prevention of altitude sickness (McKenna, 2001). It was used 160–320 mg/day (EGb 761) from day 16 of menstrual cycle to day five of the next menstrual cycle. Its adverse effects were mild: GI, confusion, dizziness, headache, constipation, and palpitations (Jurgens, 2009).

A study was conducted to determine the effect of ginkgo biloba L on the symptoms of PMS. Their single-blind, randomized, placebo-controlled trial was conducted from November 2007 to April 2008. Students who lived in dormitories of a medical university (Tehran) and suffered from PMS symptoms were selected. They recorded daily symptoms for two consecutive menstrual cycles. After 90 students with PMS were identified, they were randomized in two treatment and placebo groups and took ginkgo biloba L. tablets (containing 40 mg leaf extracts) or placebo three times a day from the 16th day of the menstrual cycle to the fifth day of the next cycle. The results showed that there were reduced physical and psychological symptoms and their severity in both groups. They concluded that ginkgo biloba L. can reduce the severity of PMS symptoms (Ozgoli, 2009).

## 2.5 Soy

A cross-sectional study was conducted to evaluate the effect of dietary soy isoflavones on PMS. In that study, 84 women between the ages of 28 and 40 years participated. They found that soy isoflavone intake was significantly related to MDQ scores in the menstrual phase. They suggested that soy isoflavones could be one of the dietary factors related to the complexity of premenstrual syndrome (PMS) and further study conducted on the effect of soy isoflavones on PMS is required (Kim, 2006).

A study was conducted to determine the effect of soy isoflavones on premenstrual symptom severity. Results indicated that premenstrual symptoms like headache and breast tenderness were reduced in the

soy IF group. After active treatment, the soy IF group showed significantly greater reduction of cramps and swelling over the placebo group (Bryant, 2005).

A cross-sectional study was conducted to evaluate the effects of intake of soy, fat, and other dietary components on premenstrual symptoms in 189 Japanese women aged 19-34. Food consumption information, including soy products and isoflavones, was obtained by a semiquantitative food frequency questionnaire. The Moos Menstrual Distress Questionnaire (MDQ) was used to evaluate the changes in the menstrual cycle. They found that soy products or isoflavone intake do not change the MDQ score in the premenstrual phase (Negata, 2004).

## 2. Discussions

Medicinal plants can be used in the treatment of premenstrual syndrome with respect of specific principles and precaution. Chasteberry is possibly effective and effectiveness of saffron, ginkgo, St. John's wort, and soy are limited according to the evidence. Therefore more studies are needed about them and other plants.

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