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## Premenstrual syndrome (PMS) and review of probable mode of action of a polyherbal medicine- prementrid

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### Abstract

Premenstrual syndrome (PMS) is a group of symptoms linked to the menstrual cycle of a woman. Changes in hormones during the menstrual cycle seem to be an important cause of PMS. The root cause of PMS is high estrogen to progesterone ratio. Prementrid® Capsule is a unique blend of phyto ingredients which act in a collective route to help reduce the symptoms of PMS. Prementrid contains an exclusive combination of four effective ingredients: *Vitex-agnus-castus* extract, *Zingiber officinalis* Extract, *Trigonella foenum-graecum* extract and *Pyrus malus* juice extract.

Premetrid capsule balances the high estrogen to progesterone ratio, inhibits production of prostaglandins and thus reduces pain, has a diuretic and spasmolytic effect and acts as a natural source of iron. Prementrid, blended with all the effective natural ingredients acts as an efficient and safe option for management of premenstrual syndrome.

**Keywords:** Pre-menstrual syndrome, vitex-agnus-castus, chaste berry, trigonella extract, prementrid

### Introduction

The menstrual cycle is the preparation of a woman's body for a possible pregnancy. This series of events occurs monthly during the woman's reproductive years (from puberty to menopause). The menstrual cycle usually lasts about 25 to 32 days. The menstrual cycle includes the activities of the hormones of the hypothalamus, the anterior pituitary gland and the ovaries, and the resulting changes in the ovaries, uterus, cervix, and basal body temperature [1, 2]. Premenstrual syndrome (PMS) or Pre-menstrual tension refers to physical and emotional symptoms that occur in one to two weeks before a woman's menstrual cycle or menstruation. Many women feel physical or mood changes during the days before menstruation. When these symptoms happen month after month, and they affect a woman's normal life, they are known as PMS. Scientifically Premenstrual syndrome is defined as recurrent moderate psychological and physical symptoms that occur during the luteal phase of menses and resolve with menstruation [3, 4].

### Premenstrual syndrome (PMS) symptoms

The identified core symptoms of PMS are: anxiety/tension, mood swings, aches, appetite/food cravings, cramps, and decreased interest in activities. These symptoms fall into three domains: emotional or psychological, physical, and behavioral. Although more than 200 symptoms have been associated with PMS, common symptoms include those listed in table 1 [5, 6].

**Table 1:** Common symptoms of Premenstrual syndrome:

Physical symptoms:	Behavioral symptoms:	Psychological symptoms:
Abdominal bloating Back pain Breast pain, tenderness, and/or swelling Headache Muscle aches Weight gain	Aggression Changes in sexual interest Dizziness Fatigue Food cravings or overeating Insomnia	Anger, Anxiety Confusion Crying and tearfulness Decreased self-esteem Depressed mood Difficulty concentrating Forgetfulness, Irritability Loneliness, Mood swings Restlessness, Tension

### Premenstrual syndrome (PMS) effects on quality of life

Symptoms induced by premenstrual syndrome (PMS) adversely affect the women in reproduction period and decrease their quality of life. It is the cause of considerable morbidity

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and the health burden has been consistently underestimated. These conditions are not life threatening but they can seriously decrease the quality of life of many women and affect their mental health and their productivity.

Problems with relationships at home and at work, parenting, and work performance are the major setbacks of PMS. Moderate to severe PMS seems to be associated with work productivity impairment and increased absenteeism, and thus poses a potential economic burden.

PMS has been shown to negatively affect relationships, work attendance, productivity, and health care costs and utilization. PMS affects women's quality of life, economic and social performance. In other study, about 23- 31% of reproductive aged women experience PMS to a degree that affects their daily lives.

A recent study of women with severe premenstrual symptoms noted that impairment of family and social activities was similar to that seen in major depressive disorder. There is also a growing evidence of an association between psychosocial stress and menses-associated health problems in women [7, 8].

### Pathophysiology of premenstrual syndrome (PMS)

#### Change in estrogen/progesterone ratio

Changes in hormones during the menstrual cycle seem to be an important factor; changing hormone levels affect some women more than others. Research has consistently shown that an increased ratio of estrogen to progesterone, with a mild to moderate excess of estrogen and deficiency of progesterone (estrogen dominance), is a common factor in most of the women affected. There are many causes of estrogen dominance. In rare cases it can be caused by a genetic abnormality. However, it usually is influenced by lifestyle choices, which women do have control over. One of the main reasons women have too much estrogen is due to estrogens that are coming into their bodies from inorganic food and environmental toxins. These are called xenoestrogens. Symptoms often vary between women and resolve around the start of bleeding. Common symptoms include acne, tender breasts, bloating, feeling tired, irritability, and mood changes.

#### Increase in prolactin secretion

Prolactin is normally produced by the pituitary gland and functions in milk production in lactating women. Some women with PMS have elevated prolactin levels, while others appear to be over sensitive to normal levels. Symptoms associated with prolactin include abdominal tension, edema, weight gain and breast tenderness.

#### Increased sensitivity to and excessive production of prostaglandins

Excessive production of prostaglandins from the endometrial tissue is seen in PMS. One of the symptoms of PMS is pain, such as backache and abdominal pain. In women with PMS, severe headache outbreaks during the luteal phase and an increase in headache resistance to painkillers and anti-inflammatory drugs lead to increase in depression, irritability, anxiety, anger, and food intolerance during the luteal phase [7, 8, 9].

#### Premenstrual syndrome (PMS) treatment options

Because the etiology of PMS is not clear, symptom relief is the goal of treatment. Treatment of PMS is best approached in

a stepwise fashion, beginning with lifestyle modifications and progressing to nutritional supplementation, nonpharmacologic therapy, and nonprescription and prescription medications.

Medications affecting serotonin are first-line pharmacologic treatments for severe PMS. The selective serotonin reuptake inhibitors (SSRIs) taken daily or only during the luteal phase of menstruation-significantly decrease physical and psychological symptoms of PMS compared with placebo. Few data support the effectiveness of oral contraceptives in treating PMS. Suppressing ovarian function with continuous oral contraceptive use may ameliorate symptoms. *GnRH Agonists* suppress ovarian function, the GnRH agonists have been tried off-label to reduce severe physical symptoms of PMS. Since PMS is cyclical and these medications have to be given periodically, long term use poses a safety warrant.

**Complementary and alternative therapies:** Botanical medicines have been used for centuries throughout the world to treat the symptoms of menstrual irregularities. Two herbal supplements have shown some evidence of effectiveness in treating PMS when taken during cycle days. Evening primrose oil is the most widely studied product; it is thought to provide a precursor for prostaglandin synthesis, but the bulk of scientific evidence does not support its usefulness. Chaste Tree Berry (*Vitex-agnus-castus*) is the herb with the best scientific documentation for its role in being specifically useful for PMS [10, 11].

#### Prementrid® capsule

Prementridis a unique blend of Phyto ingredients which act in a collective route to help reduce the symptoms of PMS. Prementrid contains an exclusive combination of four effective ingredients. These phytochemicals present in Prementridare well-chosen to minimize the PMS and regularize it due to their significant properties. These ingredients are extensively studied through numerous scientific studies for their pharmacological activity. Number of well-planned human studies are being published to support their scientific rationale.

Nowadays, more women are found to prefer non-pharmaceutical approaches including dietary changes, exercise, cognitive behavioral therapy, and complementary and alternative medicine. Prementrid capsule presents itself as a safe and natural option with best combination of herbs to treat PMS effectively.

#### Discussion

Prementrid capsule is a unique combination of four effective ingredients: *Vitex-agnus-castus* extract, *Zingiber officinalis* extract, *Trigonella foenumgraecum* extract and *Pyrus malus* juice extract.

The various chemical compounds present in the capsule acts on estrogen, progesterone and prolactin levels which are changed during PMS and regularize them to reduce the severity of the disease. Prostaglandin levels are also regulated to reduce the pain associated with PMS. Diuretic and spasmolytic effect exerted by the compounds present in the Prementrid capsule helps to relieve the spasms and other negative symptoms of PMS.

#### 2.1 Balance of estrogen: progesterone ratio

Linoleic acid and Apigenin from *Vitex-agnus-castus* present in Prementrid, act primarily to alleviate the symptoms of

premenstrual syndrome in the following manner.

These nutrients act as dopaminergic agonists, have anti-estrogenic activity and regulates LH and FSH levels.

### 2.1.1 Inhibition of Prolactin release

Linoleic acid and Apigenin act as dopaminergic agonists (acts like dopamine). Prolactin cell (also known as lactotrope) is a cell in the anterior pituitary gland which produces prolactin in response to hormonal signals. Linoleic acid and Apigenin binds to dopamine-2 receptors expressed on the cell membrane of the lactotroph, activation of which results in a reduction of prolactin exocytosis and gene expression by a variety of intracellular signalling mechanisms. This dopaminergic activity inhibits basal and thyrotropin-releasing hormone (TRH)-stimulated prolactin release by the pituitary gland. Dopamine is the physiological inhibitor of prolactin; thus, it appears this dopaminergic effect of chasteberry results in an inhibition of prolactin synthesis and release. Prolactin suppresses the corpus luteum, which leads to a reduction in progesterone production. If prolactin levels are reduced, the corpus luteum would then increase its production of progesterone [12, 13, 14, 15].

### 2.1.2 Estrogen balance

Linoleic acid and Apigenin have affinity for the estrogen receptor (ER) and appears to have affinity for the beta-subunit of the ER with no affinity for the alpha subunit. This binding activates ER band induces ERb mRNA activation. The compounds do not bind to Era and hence no increase of Estrogen-dependent Alkaline Phosphatase (indicative of estrogen city via ERa) is observed.

Thus, due to potent binding to the beta subunit of the Estrogen Receptors (ERb) and not the alpha subunit typically associated with 'estrogen-like effects', the overall action observed is of practically anti-estrogenic. This regulates the level of Progesterone and reduces premenstrual syndrome [16].

### 2.1.3 Stimulation of Lutenizing Hormone (LH)

The compounds act directly on the pituitary gland to inhibit the secretion of follicle stimulating hormone (FSH) and promote the secretion of luteinizing hormone (LH). FSH causes the granulosa and theca cells in ovarian follicles to grow and secrete a follicular fluid that contains a high concentration of estrogen. Therefore, an inhibition of FSH secretion should reduce elevated estrogen levels. LH enhances the growth of the corpus luteum, which stimulates the secretion of progesterone. Thus, Prementrid' s apparent stimulatory effect on LH leads to an increase in progesterone, which may normalize the balance between estrogen and progesterone.

Therefore, the normalizing effect of progesterone levels may also be due to its LH-stimulation effects in addition to its dopaminergic effect [17, 18].

## 2.2 Reduction of pain associated with PMS:

**Inhibition of Prostaglandins:** The compounds present in Prementrid, Gingerol and Shogaol (10-gingerol, 8-shogaol, and 10-shogaol) are obtained from *Zingiber officinalis* and Ursolic acid from *Pyrus malus* juice extract. These compounds inhibit prostaglandin synthesis and have anti-inflammatory effects and thus reduce pain associated with PMS.

The three compounds strongly inhibit the metabolism of cyclooxygenase and lipoxygenase enzymes and thereby prevent the production of prostaglandins. Cyclooxygenase

and lipoxygenase enzymes are involved in prostaglandin synthesis. It is this ability to inhibit cyclooxygenase and lipoxygenase that leads to reduction in leukotriene and prostaglandins, and consequent pain relief [19, 20, 21, 22, 23].

### 2.3 Diuretic and spasmolytic effect

Diosgenin and Trigonelline present in the product Prementrid obtained from *Trigonella foenum-graecum* have diuretic and spasmolytic effect.

Thus, these compounds may help in the management of PMS by relieving pelvic congestion, breast tenderness, and weight gain by its diuretic effect. Its spasmolytic effect through uterine stimulant activity may relive premenstrual gastrointestinal spasms.

Also, its antihistaminic effect can relive premenstrual tension. It has been proposed that inflammatory reaction occurs in two phases *viz.*, release of histamine, serotonin and bradykinin in the early or first phase, followed by the release of prostaglandin in the late or second phase. These compounds act on release, synthesis or action of the inflammatory mediators [24, 25, 26, 27, 28, 29].

### 2.4 Natural source of iron

Iron from *Pyrus malus* extract present naturally in the Prementrid capsule gets absorbed more easily in the body. Thereby it helps to reduce fatigue during PMS [30, 31].

The important ingredient of the product-Prementrid is *Vitex-agnus-castus* extract which is studied extensively in various clinical studies conducted worldwide. It has shown efficacy in single as well as in comparison with standard drugs. In a study carried out by Zamani *et al*, the therapeutic effect of *Vitex-agnus-castus* on women who had the PMS, in comparison with placebo, were investigated in Iran. *Vitex-Agnus* was found to be effective and well tolerated treatment for the relief of symptoms of mild and moderate PMS [32]. The efficacy of the extract of *Vitex-agnus-castus* (VAC, BNO 1095) in the treatment of Chinese women suffering from moderate to severe premenstrual syndrome (PMS) was assessed. *Vitex-agnus-castus* extract BNO 1095 was effective in treating moderate to severe PMS in Chinese women, especially in symptoms of negative affect and water retention [33]. In another study carried out by He Z *et al*, the efficacy and safety of VAC BNO 1095 extract in Chinese women suffering from moderate to severe premenstrual syndrome (PMS) was investigated [34]. In a systematic review aimed at analysing the effects of herb remedies in the PMS conditions, *Vitex-agnus-castus* was the more investigated remedy (four trials, about 500 women), and it was reported to consistently ameliorate PMS better than placebo. On the contrary, neither evening primrose oil nor St. John's Wort showed an effect different than placebo [35].

Another systematic review of *Vitex* extracts for premenstrual syndrome, shows effectiveness of this plant in treating PMS, seven of eight trials found *Vitex* extracts to be superior to placebo (5 of 6 studies), pyridoxine (1), and magnesium oxide (1). Despite some methodological limitations, the results from randomised, controlled trials to date suggest benefits for *Vitex* extracts in the treatment of premenstrual syndrome [36].

Prementrid contains this researched and proved plant for PMS in effective and synergistic combination with other three known plants. Thus Prementrid presents itself as the best option when it comes for PMS.

## Conclusion

Symptoms induced by premenstrual syndrome (PMS) adversely affect women and decrease their quality of life.

There is no standardized method of treating PMS. Overall, women with premenstrual disorders represent a largely uncared-for group for whom the evidence for conventional therapy is sparse and controversial. The number of women seeking treatment for premenstrual symptoms is on the increase. Conservative treatment has proved beneficial in many women and should be considered first-line therapy in women with mild symptoms and adjunctive therapy in all others.

Prementrid capsule with a perfect blend of well-studied plants available in synergistic combination presents an effective way to tackle the problem of Pre-menstrual disorders. Prementrid comes with an effective combination of Vitex-agnus-castus – scientifically proven for PMS. It naturally balances disrupted female hormones, relieves psycho-somatic symptoms of PMS & thus stabilizes the mood. Prementrid can be considered as an herbal, non-hormonal uterine tonic, with no unwanted effects, and Safe & Non-toxic option. Since there is no conventional therapy available for PMS, Prementrid fills the need gap.

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