



AORTM
Advanced Orthomolecular Research

MONOGRAPH

PRO Vitex

Hormone Normalizer



ABOUT AOR

Advanced Orthomolecular Research (AOR) is a Canadian company headquartered in Calgary, Alberta. AOR has an established reputation as the most advanced supplement formulator in the country and throughout the world. It is through ethical discipline and evidenced-based science that we lead and advance the natural health industry. For more information, please visit aor.ca.

ABOUT AOR'S PRO SERIES

The Professional Series provides unique formulations to meet the needs of health care professionals. The Professional Series is exclusive to clinicians, it is not available in any retail stores or websites. Formulations are designed to address specific clinical concerns with the appropriate forms of ingredients, sources, and dosages for therapeutic benefit in a number of disease and preventative processes. Created by practicing NDs that are guided by the latest research and clinical experience, the Professional Series still contains time-tested favourites as well as unique and innovative formulations.

AOR PRODUCT PATH

From raw material selection to manufacturing and shipping of final packaged goods, AOR adheres to the strictest of quality control standards. Our products represent innovative ideas and thoughtfully researched concepts with advanced techniques to develop products of superior quality and effectiveness - bringing you "Innovation you can trust".



SUPPLEMENT FACTS

NPN: 80059912

AOR34352 60 capsules

Serving Size
2 capsules

Medicinal Ingredients:

<i>Vitex agnus-castus</i> (Chasteberry extract).....	166.7 mg
Vitamin B6 (Pyridoxal-5'-phosphate).....	60 mg

Non-medicinal Ingredients: silicon dioxide, maltodextrin and microcrystalline cellulose.

Capsule: hypromellose, chlorophyll.

Suggested Dose: Take one capsule twice daily with food.

PRODUCT SPOTLIGHT

PRO Vitex

Hormone Normalizer



CLINICAL APPLICATIONS:

Hormonal dysregulation, to address menstrual irregularities, premenstrual syndrome (PMS), premenstrual dysphoric disorder (PMDD), mastalgia, anovulation, infertility, PCOS, acne and peri-menopause.

SUGGESTED DOSE:

Two capsules daily with or without food. Use for a minimum of three months for maximum effects.

1. SUMMARY

The Pro Vitex contains a synergistic combination of chasteberry (*Vitex agnus-castus*) and pyridoxal-5'-phosphate, the active form of vitamin B6. Vitex is a commonly known medicinal herb that has been used extensively for hormonal dysregulation, to address menstrual irregularities, premenstrual syndrome (PMS), headache, hot flashes, mastalgia, anovulation, infertility, polycystic ovarian syndrome (PCOS) and acne. Research into the pharmacodynamics of this herb reveals its dopaminergic activity reduces prolactin levels to regulate progesterone, elucidating Vitex's neuroendocrine effects to relieve psychological and hormonal symptoms related to PMS. Furthermore, recent insights into additional antinociceptive mechanisms have further revealed how Vitex effectively relieves premenstrual pain.

2. BACKGROUND

Vitex agnus-castus, commonly known as chasteberry, is part of the *Verbenaceae* family that grows within the Mediterranean region and parts of Asia.¹ Traditional uses of the whole fruit extract date back over 2,500 years, where Roman, Greek and Egyptian herbalists administered Vitex to for menstrual irregularities. Its use persisted into medieval Europe in order to reduce libido, hence its common name "chaste" berry.² Traditional uses have continued into modern day medicine as clinical studies uncover its effective use in the treatment of menstruation-related disorders.

3. CLINICAL STUDIES

3.1 PREMENSTRUAL SYNDROME

Clinical studies show the effectiveness of *Vitex agnus-castus* in both psychological and physical symptoms related to PMS.³ In a systematic review that included 12 RCT studies, the effects of Vitex on PMS, PMDD and hyperprolactinemia were evaluated.⁴ Standardized dried extracts of Vitex ranged from 20 to 40 mg per day for three to twelve months, with the highest dose reported at 1,800 mg. Eight RCTs (n=762), reported a significant improvement compared to placebo in irritability, mood alterations, anger, headache and breast fullness. In another study, a 52% response rate in the treatment group was reported compared to 24% in the placebo group.⁵ In addition, one study reported Vitex to be equivalent to the SSRI, fluoxetine, in treatment of premenstrual dysphoric disorder (PMDD).^{6,7}

3.2 CYCLICAL MASTALGIA

In a prospective study, 40 mg of standardized *Vitex agnus-castus* extract improved symptoms of cyclical mastalgia. The study involved two groups, each with 40 women who presented with mastalgia (Group 1) or hyperprolactinemia (Group 2). Each group were randomized to receive a three-month course of either a dopamine agonist, bromocriptine (2.5 mg twice daily) or a standardized extract of Vitex (40 mg daily). Serum prolactin levels reduced by 44%, from 945.66 mIU/L to 529.19 mIU/L with Vitex compared to 885.04 mIU/L to 472.68 mIU/L with bromocriptine. Using visual pain scores for mastalgia, levels decreased from 6.8 to 1.9 and 6.3 to 0.89 with vitex and bromocriptine, respectively. Nausea and vomiting were reported by 12.5% of participants administered bromocriptine, while no adverse effects were reported with Vitex.⁸ It was concluded that Vitex was comparable to bromocriptine for reducing serum prolactin levels and ameliorating cyclic mastalgia without side-effects.⁹

3.3 MELATONIN MODIFICATION

Preliminary studies show Vitex may impose a dose-dependent increase in melatonin secretions. In an open, placebo-controlled trial (n=20), daily administration of 120 mg, 240 mg or 480 mg per day of Vitex for 14 days resulted in a 163.3% increase (confidence interval = 127.8 - 208.6%, p <0.005) in nocturnal melatonin production compared to placebo.^{4,10}

4. PHARMACOLOGY

MECHANISMS OF ACTION

The main compounds extracted from the fruit of *Vitex agnus-castus* are diterpenes, flavonoids, and iridoid glycosides, are shown to exert dopaminergic, opioid and estrogenic activity. Diterpenoid compounds extracted from Vitex are dopamine receptors agonists (D2 and D3 receptors), which bind receptors within the anterior pituitary gland to reduce stress induced prolactin levels through negative inhibition. The overall effect is a reduction in mastalgia and anovulation.^{1,4} This also accounts for Vitex's indirect influence on progesterone. Elevated pituitary secretion of prolactin reduces hypothalamic production of gonadotropin-releasing hormone (GnRH) and subsequent LH and FSH levels. Low GnRH diminish follicular development and thus the formation of the corpus luteum and production of progesterone. Vitex's effect on prolactin consequently disinhibits GnRH to facilitate proper folliculogenesis and thus progesterone synthesis.

The flavonoid casticin is shown to have nociceptive effects, able to bind mu opioid receptors (MOR) to elicit the release of β -endorphins and significantly reduce symptoms of depression, irritability, anxiety, mastalgia and headaches associated with PMS.¹¹ MOR and the endogenous opioid system is shown to influence hypothalamic-pituitary-axis (HPA) activity, inhibiting noradrenergic activity and modulating GnRH levels to influence hormone levels during the menstrual cycle. An inverse correlation between severity of PMS symptoms and endogenous opioid levels have been demonstrated, further solidifying the influence of endorphins in the pathophysiology of menstrual irregularities.^{1,3}

Furthermore, recent cell culture studies reveal phytoestrogenic activity of casticin and apigenin, able to selectively bind β -estrogen receptors (ERB). Using 0.6 and 1.2 g per kg body weight dose of Vitex, animal studies show regulatory effects on fat tissue homeostasis and estrogen receptor modification. The study showed an increase in serum estrogen and progesterone that lead to an increase of vaginal cell cornification and uterine hypertrophy by 229 and 243% respectively when compared to controls.^{9,12}

Pyridoxal-5-phosphate is the active form of vitamin B6. It is used as a cofactor for dopamine and serotonin synthesis and facilitates the conversion of glutamate to GABA or alpha-ketoglutarate to improve overall mood and relaxation.¹³

5. PHARMACOKINETICS, ADVERSE EFFECTS, AND INTERACTIONS

5.1 PHARMACOKINETICS

Using an animal model, the elimination half-life of intravenous administration of 50 mg/kg of casticin was 20.86 ± 2.02 min (range 18.66–22.64 min). Plasma levels peaked at 43.83 ± 1.47 minutes with a peak concentration of 287.06 ± 40.68 ng/ml after oral administration of 400 mg/kg casticin. Limited data is available for other composites found in *Vitex agnus-castus*.¹⁴

5.2 ADVERSE EFFECTS

Generally, Vitex is well tolerated, however clinical studies report mild transient side effects. In a dose tolerance study, the effects of 120 to 480 mg was assessed. There were no changes in liver enzymes, lactate dehydrogenase, bilirubin and electrolytes; thromboplastin time was prolonged from 3 to 5% in those receiving respective doses of 240 mg and 480 mg per day. The adverse effects reported, included; allergic skin and respiratory symptoms, slight confusion, eczema with puritis, gastrointestinal upset, nausea, headache, dizziness, agitation and fatigue.¹⁵

Due to lack of human studies and undetermined effects in early pregnancy, Vitex is contraindicated during pregnancy and lactation. In addition, it is recommended to avoid in other hormone-sensitive conditions, such as breast, ovarian and uterine cancer and uterine fibroids.¹⁵ Animal studies reveal the LD50 to be 12.5 g per kg bodyweight.¹²

5.3 INTERACTIONS

In vitro studies show that 0.22 ug/mL and 0.3 ug/mL of Vitex is able to inhibit CYP2C19 and CYP3A4. These enzymes metabolize a wide variety of drugs, including anticonvulsants, anti-ulcer drugs (omeprazole) and certain antidepressants, therefore caution is recommended with concomitant use.

Although there are no reports of drug interactions, based on Vitex mechanisms of action, caution is recommended with concurrent use with dopamine agonists (bromocriptine, domperidone, pramipexole, rotigotine) and hormone therapy containing progesterone, including hormone replacement therapy (HRT) and oral contraceptives.¹⁶

6. DOSAGE

The recommended dose of Vitex is 133 mg, equivalent to two capsules per day, of dried fruit extract daily (standardized to 0.6% casticin). For optimal therapeutic effects, it is recommended to continue treatment for a minimum of three months.

7. CLINICAL APPLICATIONS

CLINICAL INDICATIONS

- Hormonal dysregulation
- Menstrual irregularities
- Premenstrual syndrome (PMS)
- Premenstrual dysphoric disorder (PMDD)
- Mastalgia
- Anovulation
- Infertility
- Peri-menopause
- Polycystic ovarian syndrome (PCOS)
- Acne

8. CONCLUSION

Clinical studies consistently show the effective use of Vitex in the treatment of menstrual irregularities. Overall, standardized extract of *Vitex agnus-castus* is well tolerated with limited side effects and may be recommended as a safe and effective first-line treatment option for cyclical mastalgia, hyperprolactinemia and PMS.

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Notes