# SAFETY AND EFFICACY OF CHASTETREE (*Vitex Agnus-Castus*) DURING PREGNANCY AND LACTATION

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## ABSTRACT

### Background
There is a lack of basic knowledge on the part of both clinicians and patients as to the indications for use and safety of herbs used during pregnancy and lactation. This is one article in a series that systematically reviews the evidence for herbs commonly used during pregnancy and lactation.

### Objectives
To systematically review the literature for evidence on the use, safety and pharmacology of chastetree, focusing on issues pertaining to pregnancy and lactation.

### Methods
We searched 7 electronic databases and compiled data according to the grade of evidence found.

### Results
In pregnancy, there is poor evidence based on theoretical and expert opinion and *in vitro* studies that chastetree may have estrogenic and progesteronic activity, uterine stimulant activity, emmenagogue activity and prevent miscarriages. In lactation, theoretical and expert opinion conflict as to whether chastetree increases or decreases lactation.

### Conclusions
Given its relatively common use amongst women of childbearing age, it is likely that some women may consume chastetree while unknowingly pregnant. Complementary and alternative medicine, midwifery and medical practitioners should be aware of this fact when prescribing chastetree to women of childbearing age, particularly when the patient is planning a family.

**Key words:** *Chastetree, vitex agnus-castus, pregnancy, lactation, breastfeeding, systematic review*

Chastetree, a deciduous shrub native to Mediterranean Europe, central Asia, and parts of India, has a long history of use dating as far back as the ancient Greeks and Romans. The Latin name for chastetree is *Vitex agnus-castus*, an allusion to its usage in the preservation of chastity. The fruits of chastetree contain a mixture of iridoids and flavonoids, and some compounds isolated from the leaves and flowers were found to be similar in chemical structure to human sex hormones.[1,2]

Chastetree has been used for centuries for a variety of gynecologic conditions, including premenstrual syndrome, cyclical mastalgia and menstrual irregularities.[3] Today, the German Commission E, a panel of experts charged with

evaluating the safety and efficacy of the herbs available in pharmacies for general use, has approved chastetree for the gynecologic conditions previously cited.[4] Medical doctors in Germany frequently prescribe chastetree to patients, and it is used commonly throughout Europe and North America.[5]

The principal activity of chastetree appears to be derived from dopaminergic compounds present in the herb that improve premenstrual mastodynia and possibly other symptoms of premenstrual syndrome.[2] Evidence indicates that an extract of chastetree binds to dopamine (D2) receptors in the hypothalamus and anterior pituitary, thereby inhibiting the release of prolactin and thus reducing corresponding mastalgia. Other endocrine effects appear to occur, including increased progesterone secretion and induction of normal formation of the corpus luteum.[6]

There are claims that chastetree may enhance female fertility. As such, there is a strong likelihood that women may take this herb while unknowingly pregnant. A crossover period of taking chastetree while pregnant may be likely, which is of concern for the fetus, given its susceptibility to teratogenic influences during the first trimester.[7] We systematically searched the literature to assess for safety, efficacy, pharmacology and drug-herb interactions of *Vitex agnus castus* with an emphasis on issues relating to pregnancy and lactation.

**Synonyms/Common Names/Related Substances**

Agnolyt, agnus castus, agnus-castus, chaste berry, chaste tree, chaste tree berry, chastetree, gattilier, hemp tree, monk's pepper, vitex, *Vitex agnus castus*[8]

**Constituents**

Essential oils: limonene, cineol, pinene and sabinene[9],

Iridoid glycosides: aucubin and agnoside[10,11]

Flavonoids: casticin, kaempferol, quercetagetin, orientin and isovitexin[9,11],

Diterpenes: vitexilactone, rotundifuran and 6-beta,7 beta-diacetoxy-13-hydroxy-labda-8,14-dien[9,10,12,13]

Essential fatty acids: oleic acid, linolenic acid, palmitic acid and stearic acid[13]

**Part used**

Fruit[14]

## METHODS

In keeping with the principles of evidence-based practice, we endeavoured to identify and analyse all the relevant scientific medical literature that provided information as to the safety, efficacy and pharmacology of chastetree in pregnancy and lactation. We searched the following databases from inception to June 2006: AMED, CINAHL, Cochrane CENTRAL, Cochrane Library, MedLine, Natural Database and Natural Standard. The common and Latin names of the herb were used as key words along with "pregnancy", "lactation" and "breastfeeding". In addition, we searched the Complete German Commission E Monographs by the American Botanical Council.

Each relevant journal article was collected and referenced in our database. The nature of the findings and the grade of evidence were then abstracted and compiled in our final report. The grade of evidence for indications was evaluated as displayed in Table 1. We rated evidence of harm as displayed in Table 2.

## RESULTS

**Indications for Use**

| | Evidence Grade |
|---|---|
| Premenstrual syndrome[11,15-20] | B1 |
| Cyclic mastalgia[21,22] | B1 |
| Hyperprolactinemia[23] | B1 |
| Infertility (homeopathic preparation)[24] | B1 |
| Infertility[11,13,25] | B2 |
| Acne[11] | E |
| Menstrual disorders[11,17] | E |

**Use and Safety during Pregnancy**

| | Level of evidence for potential harm |
|---|---|
| Increases progesterone (homeopathic preparation)[24] | 1 |
| Estrogenic and progesteronic activity[26] | 5 |
| Uterine stimulant[8] | 5 |
| Emmenagogue[27] | 5 |
| Prevention of miscarriages[11] | 5 |

A prospective, randomized, placebo-controlled, double-blind study was conducted on a homeopathic preparation of chastetree for women with fertility disorders.[24] The researchers observed a non-significant increase in fertility and a significant increase of progesterone during the luteal phase.[24] Lower level evidence using chastetree as a herbal preparation also indicates that it may have estrogenic and progesterone activity.[26]

Compendia of drug interactions and safety on natural products report that chastetree is a uterine stimulant and an emmenagogue.[7,8] However, our search of the evidence-based literature found no reports of chastetree being a uterine stimulant or an emmenagogue.

A compendium on herbal medicine reported that chastetree is used by some clinicians during the first trimester of pregnancy to prevent miscarriages in patients with progesterone deficiency.[11] No reports in the peer reviewed medical literature indicate that chastetree actually prevents miscarriages through this, or any other, mechanism.

### Use and Safety during Lactation

| | Level of evidence for potential harm |
|---|---|
| Increases lactation[9,11,13] | 5 |
| Decreases lactation[17] | 5 |

Compendia on herbal medicine and a plant monograph report that chastetree increases lactation.[9,11,13] There was one additional source reporting that chastetree decreases lactation due to the suppression of prolactin production.[17]

### Toxicity and Adverse Effects

In a recently conducted systematic review of adverse events of chastetree used as single treatment, it was found that side effects potentially caused by *Vitex agnus castus* were mild and reversible.[28] The most frequently cited adverse events include: nausea, mild gastrointestinal complaints, fatigue, menstrual disorders, dry mouth, acne, pruritus and erythematous rash.[5,28] There was one report of a case of nocturnal seizures in a patient taking a combination of herbs that included chastetree, however, it is unlikely that *Vitex* was the causative agent.[5,29]

### Pharmacology

There is some evidence that chastetree may have hormonal properties through estrogenic and progesterone activity, however, the evidence is limited.[26] It is claimed that compounds in chastetree selectively bind to beta estrogen receptors in the heart, vasculature, bone and bladder.[2] Chastetree may affect dopamine, acetylcholine and opioid receptors.[12] In high doses, chastetree has agonist effects on pituitary dopamine (D2) receptors.[1,30] In women with hyperprolactinemia, evidence suggests that chastetree suppresses prolactin release and normalizes luteal phase defects in the menstrual cycle.[23]

Chastetree does not appear to affect testosterone levels.[31] *In vitro* work suggests that *Vitex* may inhibit the growth of breast, ovarian, cervical, gastric, colon and lung cancer cells.[32,33] Essential oils derived from this herb have demonstrated antibacterial and antifungal properties.[11]

### Drug Interactions

The likelihood of drug interactions resulting from chastetree consumption is relatively low. However, this herb is contraindicated for use in conjunction with drugs used to treat Parkinson's disease, such as bromocriptine and metaclopramide.[2,30] In addition, concurrent use of antipsychotic drugs is contraindicated[1,30], as are any dopamine agonists.[1,12,30] Caution is suggested with oral contraceptives and during hormone replacement therapy.[34]

## DISCUSSION

There is strong scientific evidence that chastetree may be beneficial for the treatment of premenstrual syndrome, cyclical mastalgia and hyperprolactinemia. There is good scientific evidence of efficacy for the treatment of infertility. As an ingredient of a homeopathic preparation, chastetree was not shown to be significantly effective in treating infertility, but did increase progesterone secretion.

In pregnancy, there is poor evidence based on theoretical and expert opinion and *in vitro* studies that chastetree may have estrogenic and progesteronic activity, uterine stimulant activity, emmenagogue activity and prevent miscarriages.

As such, the safety of chastetree during pregnancy remains unclear until human studies are conducted to validate its safe use for both the mother and unborn child. Given its relatively common use amongst women of childbearing age, it is likely that some women may consume chastetree while unknowingly pregnant, as approximately half of all pregnancies are unplanned. Complementary and alternative medicine, midwifery and medical practitioners should be aware of this fact when prescribing chastetree to women of childbearing age, particularly when the patient is planning a family.

In the case of lactation, theoretical and expert opinion conflict as to whether chastetree increases or decreases lactation. There are no reports in the scientific literature to suggest that compounds from this herb cross into the breast milk. The low toxicity profile and tolerability of chastetree makes it unlikely to be toxic for the newborn, especially after filtration and dilution through the mother. Nonetheless, caution is warranted with its use as chastetree has phytoestrogenic and phytoprogesteronic properties. More human research is warranted to determine the action of chastetree on breast milk production; until then, it should be used with caution.

Further research should focus on the pharmacokinetics of this herb, as well as to what degree constituents are able to cross the placental barrier into the fetus and cross into breast milk. This herb appears safe for general use, but it is important that we know more regarding its level of safety and possible therapeutic roles with respect to the breastfeeding mother and, especially, the expectant mother.

**TABLE 1** Levels of Evidence for Efficacy

| GRADE | LEVEL OF EVIDENCE |
|---|---|
| A | **VERY STRONG SCIENTIFIC EVIDENCE**<br>Statistically significant evidence of benefit from one or more systematic reviews/ meta-analysis. |
| B1 | **STRONG SCIENTIFIC EVIDENCE**<br>Statistically significant evidence of benefit from one or more properly conducted random control trials (RCTs). |
| B2 | **GOOD SCIENTIFIC EVIDENCE**<br>Statistically significant evidence of benefit from one or more RCTs. The RCTs, however, are either of small sample size OR have discrepancies in their methodologies. |
| C | **WEAK SCIENTIFIC EVIDENCE**<br>Statistically significant evidence of benefit from one or more cohort studies OR case control studies. |
| D | **VERY WEAK SCIENTIFIC EVIDENCE**<br>Evidence from case series OR case reports. |
| E | **INDIRECT EVIDENCE**<br>Expert opinion OR laboratory studies. |
| F | **HISTORICAL OR TRADITIONAL EVIDENCE**<br>Historical or traditional use by medical professionals, herbalists, scientists or aboriginal groups. |

**TABLE 2** Levels of Evidence for Harm

| LEVEL | EVIDENCE |
|---|---|
| 1 | **STRONG SCIENTIFIC EVIDENCE**<br>Statistically significant evidence from one or more systematic reviews or RCTs. |
| 2 | **ACCEPTABLE SCIENTIFIC EVIDENCE**<br>Statistically significant evidence from one or more well designed cohort studies OR case control studies. |
| 3a | **WEAK SCIENTIFIC EVIDENCE**<br>Evidence from one or more case series. |
| 3b | **VERY WEAK SCIENTIFIC EVIDENCE**<br>Evidence based on case reports. |
| 4 | **INDIRECT SCIENTIFIC EVIDENCE**<br>Evidence based on scientific studies conducted on animals, insects or microorganisms OR laboratory studies on human cells. |
| 5 | **THEORETICAL EVIDENCE**<br>Evidence based on scientific theory OR expert opinion. |
| 6 | **UNKNOWN**<br>No available information. |

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