

Chasteberry

BEATRIX ROEMHELD-HAMM, M.D., PH.D., *University of Medicine and Dentistry of New Jersey-
Robert Wood Johnson Medical School, New Brunswick, New Jersey*

For centuries, chasteberry has been used to treat many hormone-related gynecologic conditions. The current literature supports the use of chasteberry for cyclical breast discomfort and premenstrual syndrome; data on its use for menstrual irregularities and fertility disorders are weak. Its traditional use as a galactagogue (i.e., a substance that enhances breast milk production) is not well supported in the literature and should be discouraged. There are no clinical data to support the use of chasteberry for reducing sexual desire, which has been a traditional application. Chasteberry is well tolerated; reported adverse effects are minor and may include gastrointestinal complaints, dizziness, and dry mouth. No herb-drug interactions have been reported, but caution is advised for its concomitant use with dopamine agonists or antagonists. Optimal standardization and dosing recommendations await clarification in clinical studies. (*Am Fam Physician* 2005;72:821-4. Copyright© 2005 American Academy of Family Physicians.)

Chasteberry (*Vitex agnus-castus*), or monk's pepper, is the fruit of the chaste tree. It is native to western Asia and southwestern Europe, and is now common in much of the southeastern United States.

Chasteberry has been used for more than 2,500 years to treat various conditions. In ancient Egypt, Greece, and Rome, it was used for a variety of gynecologic conditions. In medieval Europe, chasteberry was popular among celibate clergymen for its purported ability to reduce unwanted sexual libido.¹ Over the past 50 years, chasteberry has been used widely in Europe for gynecologic conditions such as premenstrual syndrome (PMS), cyclical breast discomfort, menstrual cycle irregularities, and dysfunctional uterine bleeding. The German Commission E approves the use of chasteberry for irregularities of the menstrual cycle, cyclical breast discomfort, and PMS,² and it is widely prescribed by family physicians and gynecologists in Germany.³

Pharmacology

The berry of the chaste tree contains a number of active constituents: flavonoids (i.e., casticin, kaempferol, orientin, quercetagetin, and isovitexin), iridoid glycosides (i.e., agnuside and aucubin), and essential oils (i.e., limonene, cineol, pinene, and sabinene).⁴⁻⁸ Chasteberry shows central dopaminergic activity *in vitro*^{9,10} and *in vivo*.¹¹ This dopaminergic effect inhibits basal- and

thyrotropin-releasing hormone-stimulated prolactin release.^{10,11}

Chasteberry's therapeutic effects are attributed to its indirect effects on various hormones, especially prolactin and progesterone. This hormonal effect appears to be dose-dependent: low doses of extract have resulted in decreased estrogen levels and increased progesterone and prolactin levels, possibly caused by an inhibition of the release of follicle-stimulating hormone (FSH) and stimulation of luteinizing hormone (LH) levels.^{4,7,12} However, in some studies of persons receiving higher doses, FSH and LH levels remained unchanged,^{4,10,12} while prolactin release was decreased.^{4,12} These effects may explain why lower doses of the herb might stimulate breast milk production, whereas higher doses seem to have the opposite effect.

Uses and Efficacy

Over the past 50 years, 30 European trials of chasteberry (mostly uncontrolled or unblinded) have reported improvement of menstrual and menstruation-related disorders.¹³ During the past 10 years, a few small, but high quality, double-blind randomized controlled trials (RCTs) have examined various effects of chasteberry.

PMS AND CYCLICAL BREAST DISCOMFORT

In clinical trials for the treatment of PMS, chasteberry reduced some symptoms, especially breast pain or tenderness, edema,

SORT: KEY RECOMMENDATIONS FOR PRACTICE

<i>Clinical recommendation</i>	<i>Evidence rating</i>	<i>References</i>
Chasteberry is not recommended for enhancement of milk production, modification of libido, or enhancement of fertility due to lack of evidence of effectiveness.	B	4, 7, 12, 25-27
Evidence suggests that chasteberry is effective for relieving symptoms of premenstrual syndrome.	B	15, 16, 18, 22, 23
Chasteberry may be effective in patients with cyclical breast discomfort.	B	19, 20

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, see page 736 or <http://www.aafp.org/afpsort.xml>.

constipation, irritability, depressed mood, anger, and headache.^{4,14-20}

Numerous double-blind RCTs have evaluated different chasteberry preparations for treating the symptoms of PMS. Two trials were of lesser quality^{19,20} and found little difference or small improvement of breast pain. A recent higher-quality, prospective double-blind RCT¹⁵ showed significant improvement in self-assessed symptoms associated with PMS and in physician-assessed clinical global impressions scores measuring severity of condition, global improvement, and overall benefit versus risk ($P = .001$; number need to treat = 4). The study, which specifically addressed breast fullness but not pain, involved 170 women with a diagnosis of PMS who received a standardized extract of chasteberry fruit (Ze 440, standardized to casticin) or placebo for three menstrual cycles. More than one half of the women experienced a 50 percent or greater reduction

in symptoms. Patient acceptance was high, and side effects were few and mild.¹⁵ Another placebo-controlled, double-blind trial²¹ of 104 women examined the effects of two forms of chasteberry (liquid and tablet) for at least three menstrual cycles. The women in the treatment group showed improvement of cyclical breast discomfort.²¹

A previous study¹⁶ found comparable efficacy for chasteberry and vitamin B₆, both of which decreased symptoms by almost 50 percent. This study was placebo controlled, but not double blinded, and was of suboptimal sample size. Three open trials^{18,22,23} involving between 400 and 1,600 patients also showed significant improvement of various PMS symptoms but were not controlled and were of lesser quality.

MENSTRUAL DISORDERS, AMENORRHEA, AND FERTILITY

Patients use chasteberry for a variety of menstrual irregularities and fertility disorders;^{14,24} in Germany, physicians prescribe the herb for luteal phase disorders.

Results of a small RCT²⁵ involving 96 women with fertility disorders (38 women with secondary amenorrhea, 31 with luteal insufficiency, and 27 with idiopathic infertility) suggested that patients receiving chasteberry achieved pregnancy more readily than did women in the placebo group. The subjects received chasteberry or placebo twice daily for three months. Hormone levels did not differ, but in women with amenorrhea or luteal insufficiency, pregnancy occurred in the active treatment group more than twice as often as in the group receiving placebo. However, the total number of patients conceiving was small (15 women), the treatment was only administered for three months, and the product used (Mastodynon, not currently available in the United States) contains five additional herbs that are not approved by the German Commission E reports.²

In another small RCT²⁶ involving 52 patients with luteal phase defects, women in the active treatment group were found to have reduced prolactin release, normalized luteal phases, improved luteal phase progesterone synthesis, and increased luteal phase estradiol. This

The Authors

BEATRIX ROEMHELD-HAMM, M.D., PH.D., is associate professor in the Department of Family Medicine at the University of Medicine and Dentistry of New Jersey (UMDNJ)-Robert Wood Johnson Medical School, New Brunswick. Dr. Roemheld-Hamm also serves as medical director of the Studio for Integrative Medicine of the Robert Wood Johnson University Medical Group in New Brunswick. She received her medical degree from the University of Heidelberg School of Medicine, Heidelberg, Germany, and her doctorate from the University of Mannheim, Germany. She completed a family practice residency at UMDNJ-Robert Wood Johnson Medical School.

Address correspondence to Beatrix Roemheld-Hamm, M.D., Ph.D., Department of Family Medicine, University of Medicine and Dentistry of New Jersey-Robert Wood Johnson Medical School, 1 Robert Wood Johnson Dr., MEB #256, New Brunswick, NJ 08901 (e-mail: hammbr@umdnj.edu). Reprints are not available from the author.

study appears to support the use of chasteberry for luteal phase disorders, but the actual effect on fertility was not mentioned. A recent double-blind placebo-controlled pilot study²⁷ of 30 women showed an increasing trend in midluteal phase progesterone level and an increased number of pregnancies in the 15 women who took a nutritional supplement containing chasteberry for five months.

LACTATION AND LIBIDO

There is insufficient evidence to support chasteberry's traditional use to enhance breast milk production (i.e., as a galactagogue). Some evidence suggests that low doses might increase milk production in women who are lactating.^{4,7} A small study¹² involving 20 healthy men showed increased prolactin levels in those receiving a low dose of chasteberry (120 mg per day) but a decrease of prolactin secretion with higher doses (480 mg per day).

Chasteberry also has been used to modify libido, most often to reduce sexual desire,²⁸ but sometimes to improve decreased libido.⁴ However, no clinical data exist to support these indications.

Interactions, Adverse Effects, and Contraindications

There are no reported drug interactions with chasteberry, but given its dopaminergic effects, the herb could theoretically interfere with the actions of medications for Parkinson's disease, such as bromocriptine (Parlodel) and metoclopramide (Reglan).^{10,11}

Chasteberry usually is well tolerated, with only minor adverse effects reported; in many studies these effects are similar to placebo. Side effects generally are dopaminergic in nature and may include mild gastrointestinal complaints, dizziness, headache, tiredness, and dry mouth.^{6,10,11,29-31} One report³² described a case of nocturnal seizures in a patient taking black cohosh, evening primrose oil, and chasteberry; however, a causal relationship with chasteberry is doubtful.

The use of chasteberry during pregnancy is contraindicated, and its use during lactation is controversial. Until further studies have been conducted, its use to support lactation should be discouraged.

Dosage and Preparations

The dosages and preparations of chasteberry used in different clinical trials vary widely. In many studies, 4 mg per day of an extract standardized to 6 percent of the constituent agnuside has been used. In the United States, this formulation is available as Femaprin from Nature's Way.

Dosage of the fruit extract is 20 to 40 mg per day,^{2,15} although higher doses (up to 1,800 mg per day) also have been used.⁴ Fluid extract (40 drops daily)⁴ and tincture (35 to 45 drops, three times daily) also have been used.⁵

Final Comment

The few existing high-quality clinical studies on chasteberry are small or of limited duration, which limits the ability to apply the findings to a larger population. Evidence appears to support the use of chasteberry for symptoms of PMS and cyclical breast discomfort, with some preliminary evidence for infertility. Evidence for its use in other conditions remains inconclusive.

Chasteberry is well tolerated, with few side effects and no reported herb-drug interactions. Recommended dose and treatment regimens vary depending upon brand, formulation, and anecdotal experience; optimal standards await clarification in clinical studies. *Table 1* lists the efficacy, safety, tolerability, and cost of chasteberry.

TABLE 1
Key Points About Chasteberry

Efficacy	Cyclical breast discomfort: possibly effective Premenstrual syndrome: possibly effective Fertility disorders: possibly effective based on preliminary evidence Modification of libido: insufficient evidence Stimulating lactation: insufficient evidence
Adverse effects	Infrequent: mild gastrointestinal complaints, dizziness, headache, tiredness, and dry mouth
Interactions	No significant reports of herb-drug interactions
Dosage	Varies depending on brand and formulation (available in liquid form, capsules, and tablets)
Cost	\$7 to \$14 for three- to four-week supply, depending on brand
Bottom line	A safe, well-tolerated herbal medicine that may be effective in treatment of cyclical breast discomfort and premenstrual syndrome

Author disclosure: Nothing to disclose.

REFERENCES

1. Czygan FC, Mayer JG. *Vitex agnus-castus* L, der oder das Keuschlamm. Ein kulturhistorischer essay [in German]. Accessed online March 25, 2005 at: <http://www.klostermedizin.de/html/moenschspfeffer.html>.
2. Blumenthal M. German Federal Institute for Drugs and Medical Devices. Commission E. Herbal Medicine: expanded Commission E monographs. 1st ed. Newton, Mass.: Integrative Medicine Communications, 2000.
3. Schilcher H. Phytotherapy and classical medicine. *Journal of Herbs, Spices, and Medicinal Plants* 1994;2:71-80.
4. Mills S, Bone K. Principles and practice of phytotherapy: modern herbal medicine. Edinburgh: Churchill Livingstone, 2000.
5. Upton R. Chaste tree fruit: *Vitex agnus-castus*: standards of analysis, quality control, and therapeutics. American Herbal Pharmacopoeia and therapeutic compendium. Santa Cruz, Calif.: American Herbal Pharmacopoeia, 2001.
6. Schulz V. Rational phytotherapy: a physician's guide to herbal medicine. 3d ed. Berlin: Springer, 1998.
7. Brown D. *Vitex agnus castus* clinical monograph. Quarterly Review of Natural Medicine 1994;2:111-21.
8. Jellin JM, Gregory P, Batz F, Hitchens K, et al, eds. Pharmacist's letter/prescriber's letter. Natural Medicines Comprehensive Database. 3d ed. Stockton, Calif.: Therapeutic Research Faculty, 2000.
9. Meier B, Berger D, Hoberg E, Sticher O, Schaffner W. Pharmacological activities of *Vitex agnus-castus* extracts in vitro. *Phytomedicine* 2000;7:373-81.
10. Jarry H, Leonhardt S, Gorkow C, Wuttke W. In vitro prolactin but not LH and FSH release is inhibited by compounds in extracts of *Agnus castus*: direct evidence for a dopaminergic principle by the dopamine receptor assay. *Exp Clin Endocrinol* 1994;102:448-54.
11. Wuttke W. Dopaminergic action of extracts of *Agnus Castus*. *Forschende Komplementarmedizen* 1996;3:329-30.
12. Merz PG, Gorkow C, Schrodter A, Rietbrock S, Siender C, Loew D, et al. The effects of a special *Agnus castus* extract (BP1095E1) on prolactin secretion in healthy male subjects. *Exp Clin Endocrinol Diabetes* 1996;104:447-53.
13. Rotblatt M, Ziment I, eds. Evidence-based herbal medicine. Philadelphia: Hanley & Belfus, 2002.
14. Blumenthal M. German Federal Institute for Drugs and Medical Devices. Commission E. The complete German Commission E monographs: therapeutic guide to herbal medicines. Austin, Tex.: American Botanical Council, 1998.
15. Schellenberg R. Treatment for the premenstrual syndrome with *agnus castus* fruit extract: prospective, randomised, placebo controlled study. *BMJ* 2001;322:134-7.
16. Lauritzen C, Reuter HD, Repges R, Bohnert KJ, Schmidt U. Treatment of premenstrual tension syndrome with *Vitex agnus castus*. Controlled, double-blind study versus pyridoxine. *Phytomedicine* 1997;4:183-9.
17. Berger D, Schaffner W, Schrader E, Meier B, Brattstrom A. Efficacy of *Vitex agnus castus* L. extract Ze 440 in patients with pre-menstrual syndrome (PMS). *Arch Gynecol Obstet* 2000;264:150-3.
18. Loch EG, Selle H, Boblitz N. Treatment of premenstrual syndrome with a phytopharmaceutical formulation containing *Vitex agnus castus*. *J Womens Health Gend Based Med* 2000;9:315-20.
19. Turner S, Mills S. A double-blind clinical trail on a herbal remedy for premenstrual syndrome: a case study. *Complement Ther Med* 1993;1:73-7.
20. Halaska M, Raus K, Beles P, Martan A, Paithner KG. Treatment of cyclical mastodynia using an extract of *Vitex agnus castus*: results of a double-blind comparison with a placebo [in Czech]. *Ceska Gynekol* 1998;63:388-92.
21. Wuttke W, Splitt G, Gorkow C, et al. Treatment of cyclical mastalgia: results of a randomised, placebo-controlled, double-blind study [in German]. *Geburtshilfe Frauenheilkd* 1997;57:569-74.
22. Peteres-Welter C, Albrecht M. Menstrual abnormalities and PMS. *Vitex agnus-castus* in a study of application. *Therapiewoche Gynäkol* 1994;7:49-52.
23. Dittmar F, Böhnert K, Peeters M, et al. Premenstrual syndrome: treatment with a phytopharmaceutical. *Therapiewoche Gynäkol* 1992;5:60-8.
24. Tyler VE. Herbs of choice: the therapeutic use of phyto-medicinals. New York: Pharmaceutical Products Press, 1994.
25. Gerhard I, Patek A, Monga B, Blank A, Gorkow C. Mastodynon (R) bei weiblicher Sterilität. *Forsch Komplementarmed* 1998;5:272-8.
26. Milewicz A, Gejdel E, Sworen H, Sienkiewicz K, Jedrzyjak J, Teucher T, et al. *Vitex agnus castus* extract in the treatment of luteal phase defects due to latent hyperprolactinemia. Results of a randomized placebo-controlled double-blind study [in German]. *Arzneimittelforschung* 1993;43:752-6.
27. Westphal LM, Polan ML, Trant AS, Mooney SB. A nutritional supplement for improving fertility in women: a pilot study. *J Reprod Med* 2004;49:289-93.
28. Facts and comparisons. The review of natural products (electronic resource). St. Louis, Mo.: Facts and Comparisons, 2000.
29. Newall CA, Anderson LA, Phillipson JD. Herbal medicines: a guide for health-care professionals. London: Pharmaceutical Press, 1996.
30. McCaleb R, Leigh E, Morien K. The encyclopedia of popular herbs: your complete guide to the leading medicinal plants. Roseville, Calif.: Prima Health, 2000.
31. McGuffin M. American Herbal Products Association's botanical safety handbook. Boca Raton, Fla.: CRC Press, 1997.
32. Shuster J. Black cohosh root? Chasteberry tree? Seizures! *Hospital Pharmacy* 1996;31:1553-4.