CHASTETREE

Vitex agnus-castus L.

Family

Lamiaceae (or Labiatae), the mint or sage family (former Verbenaceae).

Parts Used

Fruit.

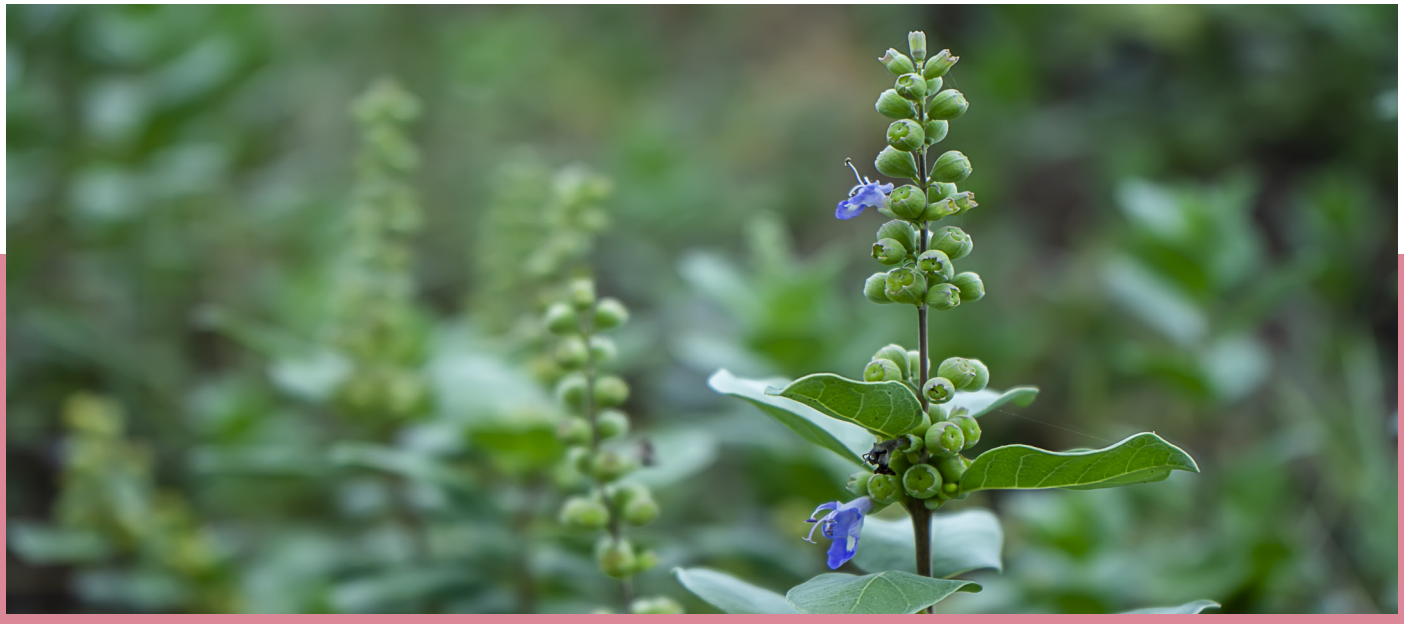
Description

A beautiful deciduous shrub or tree native to Mediterranean Europe, central Asia and parts of India, chastetree grows up to six metres tall. The undersides of its five to seven lobed leaves, and its branches, are white felted. It bears spikes of small, fragrant rose-lavender flowers arranged in whorls along the flower head. Although sometimes referred to as berries (peppercorn-like) the dark purple to red fruits are drupes (stone fruit) with a single seed.[1]

Traditional Use

Chastetree preparations have been used for centuries to treat gynaecological problems and specifically premenstrual complaints. Nearly 2000 years ago Dioscorides wrote in his Materia Medica that its use brings on menstruation, helps childbirth, increases milk production and that larger doses of it can bring on sleep.[2]

Chastetree, as the name suggests, was used in older times as a symbol of chastity, and to suppress libido, although the mode of action was not known. The specific name also refers to this: Agnós, as well as castus, mean chaste or pure. The dried fruits have a peppery taste and were used in monasteries as a condiment because they were considered to be helpful to medieval monks in keeping their vow of celibacy. A common name for chastetree even today is monk's pepper. It was



also used paradoxically for impotence. In his seminal textbook, *The New Holistic Herbal*, David Hoffmann describes chastetree as an amphoteric remedy because "it can produce apparently opposite effects though in truth it is simply normalising. It has for instance a reputation as both an aphrodisiac and an anaphrodisiac. It will always enable what is appropriate to occur".[3,4,5,6,7]

Chastetree was revered for many ailments such as colic, gas and other digestive problems in areas where it grew naturally, namely around the Mediterranean area. It had a strong reputation in England, carried through for centuries, where it was considered useful for the above conditions based on the writings of the Greeks and Romans. The English began to lose interest in it about the 1700s and did not get excited about it again until the mid-1900s, at which time it became known as a valuable herb for female reproductive imbalances. For example, chastetree cannot be found in any of the English herbals from the early 1900's, such as Leyel's Herbals or Potter's. Maude Grieve, in her famous *A Modern Herbal* (1931), gives chastetree a short paragraph saying that "the fresh ripe berries are pounded to a pulp and used in the form of a tincture for the relief of paralysis, pains in the limbs, weakness, etc".[8]

During the 1940s and 1950s considerable research work was done in Germany on the pharmacology of chastetree. This pointed to an effect on pituitary hormone activity, with an apparent effect in mimicking the activity of the corpus luteum, which is a transitional endocrine gland left in the ovary for about 10 days after ovulation. Changes in women's endometrium, basal temperature and vaginal secretions were confirmed along with lactation promoting properties.[9]

Chastetree has been called the "most archetypal" of all female reproductive herbs. Highly regarded British herbalist Anne McIntyre says chastetree has a normalising effect on female hormone balance by its effect on follicle stimulating hormone, and luteinising hormone, produced by the anterior pituitary gland. "It acts to support the corpus luteum of the ovaries in its work of producing hormones in the second half of the cycle. In practice it appears to have a more progesteronic than oestrogenic action, "she says.[10]

Founding father of modern German phytotherapy Rudolph Weiss says chastetree's indications are primarily menstrual disorders due to corpus luteum insufficiency such as heavy menstrual bleeding and abnormal uterine bleeding. He also cites acne, premenstrual herpes simplex and water retention.[11]

McIntyre adds premenstrual syndrome (PMS), irregular and painful periods, fibroids, to re-establish hormone balance after stopping use of the oral contraceptive pill, menopausal problems and stimulating milk production in nursing mothers. Women's health specialist Ruth Trickey says that although chastetree has been shown to stimulate ovulation it has not proven to be a reliable herb for polycystic ovary syndrome (PCOS).[12,13]

Menstruation is governed by two distinct cycles: the first 14 days represent the follicular phase (onset of menstruation to ovulation) and the last 14 days the luteal phase (ovulation to menstruation). In the follicular phase oestrogen rises and in the luteal phase progesterone is the rising force. Ruth Trickey says chastetree is the primary herb for problems associated with the luteal phase. Trials have verified its use in dysfunctional uterine bleeding, endometrial hyperplasia, anovulatory cycles and polymenorrhoea (a menstrual cycle that is shorter than 21 days).[14,15]

Chastetree has been used since ancient times as a galactagogue to promote milk production, especially in the first 10 days after delivery. Currently there are no double-blind studies to confirm its efficacy however an early uncontrolled study provides some support for its use in lactation finding a favourable effect on milk production in 80% of women. Current research suggests it should only be used in low doses for breastfeeding (see Contraindications and cautions).[16]

Constituents

Essential oils (limonene, sabinene, 1,8-cineole [eucalyptol]), iridoid glycosides (agnuside, aucubin), diterpines (vitexilactone, rotundifuran), flavonoids (apigenin, casticin, orientin, isovitexin), terpenoids (viteagnusins A to E), neolignans, phenolic compounds, glyceride and essential fatty acids (linoleic acid). According to a German survey, an alcohol extract of the whole berry is more efficacious than isolates of individual constituents.[17,18,19]

Actions

Hormone regulator, female tonic, uterine tonic, galactagogue.

Pharmacological Activity

There are numerous clinical trials which have assessed the safety and efficacy of various chastetree extracts for the treatment of acne, corpus luteum insufficiency, cyclic breast pain, hyperprolactinaemia (excess prolactin), menopausal symptoms, increasing lactation, PMS, uterine bleeding disorders and miscellaneous menstrual irregularities. A review of all the clinical data on chastetree is beyond the scope of this monograph. Uncontrolled trials with chastetree go back to the 1940s however the most recent and relevant studies have been included in this monograph to demonstrate efficacy. There is a dearth of whole herb ethanol studies, with most studies investigating standardised products. As with all herbal remedies a variety of chastetree preparations are used in practice which can differ substantially in terms of, for instance, concentration of active ingredients or bioavailability. A survey, more than 20 years ago, of members of the National Institute of Medical Herbalists showed that the tincture is the most popular preparation among herbalists, but liquid extracts and powdered herb preparations are also common. They said a standardised solid extract of chastetree was rarely used by herbalists then. Combination herb studies are not included in this monograph, however notable herbs which have been used in combination with chastetree in research include St. John's wort *(Hypericum perforatum)* and black cohosh *(Actaea racemosa)*.[20]

Curiously, for more than 30 years the conventional wisdom promoted in literature and product information was that chastetree corrected a clinical situation of oestrogen excess, or relative progesterone deficiency, by acting on the pituitary to increase lutenising hormone (LH) and decrease follicle-stimulating hormone. The apparent basis for this thinking was interpretations of early pharmacological research based on animal studies. Later research has challenged this perspective demonstrating the fact that although *in vivo* studies facilitate experimentation caution must be taken in extrapolating results to human clinical situations as many factors are acting upon this process.[21]

While the mode of action of chastetree is not yet completely understood it is now assumed that it has dopaminergic effects in the anterior pituitary resulting in changes of prolactin secretion. Some studies have suggested a dose-dependent effect, as lower doses (120mg) were found to increase dopamine secretion while higher doses (240 to 480mg) were found to decrease secretion. It is likely that this mechanism is responsible for the symptom-relieving effects seen with chastetree in hyperprolactinaemia and provides some rationale for its use by herbalists in disorders complicated by hyperprolactinaemia, such as amenorrhoea, mastalgia or PCOS.[22]

One study has shown it can normalise progesterone levels in women with hyperprolactinaemia within three months, while another has suggested it can stimulate progesterone receptor expression. Recent research has suggested that chastetree may exert activity in the opiate system, and the activation of mood regulatory and analgesic pathways via this system may be at least partly responsible for its efficacy in menstrual disorders.[23,24]

The treatment of broader menstrual disorders focuses on hormone normalisation often through modulation of the hypothalamic-pituitary-ovarian (HPO) axis. While chastetree was initially thought to work on increasing progesterone levels, or decreasing prolactin, research is suggesting it has a role even further upstream on the HPO axis due to its dopaminergic action.[25]

Mastalgia Activity

A 2020 systematic review and meta-analysis on chastetree for the treatment of cyclic mastalgia found that it is a safe and effective treatment option although more high-quality clinical trials are needed to strengthen the evidence base. The researchers said cyclic mastalgia is premenstrual breast pain that presents cyclically and affects women in their reproductive years. "It may associate with latent hyperprolactinaemia due to the insufficient inhibitory effect of dopamine on the pituitary gland." The review included 25 studies (17 randomised control trials plus eight nonrandomised trials). Chastetree was effective in relieving breast pain intensity and lowering the increased serum prolactin level in reproductive age cyclic mastalgia patients (18 to 45 years) with or without premenstrual

syndromes. The typical dose was 20 to 40mg a day with a treatment duration of three months. The meta-analysis included six studies and revealed a moderate effect favouring chastetree over a placebo. Seven trials demonstrated chastetree to be a noninferior alternative to pharmaceutical therapies for cyclic mastalgia, including dopamine agonists, nonsteroidal anti-inflammatory drugs, selective serotonin reuptake inhibitors (SSRIs) and hormonal contraceptives. Chastetree was safe and associated with only mild and reversible adverse events. However, the risk of bias in most studies was unclear due to insufficient information.[26]

PMS and Premenstrual Dysphoric Disorder (PMDD) Activity

A 2019 meta-analysis of double-blind randomised controlled trials assessed the use of chastetree in PMS. Out of the 21 clinical trials, three studies (520 females) fulfilled the inclusion criteria, comparing the efficacy of chastetree extracts to a placebo for the treatment of PMS. Chastetree preparations were confirmed to be effective in the reduction of PMS symptoms: women taking it were 2.57 times more likely to experience a remission in their symptoms compared to those taking the placebo. Although numerous clinical trials have been carried out with chastetree the majority of the studies cannot be used as evidence for efficacy due to incomplete reporting, especially concerning the description of the used medication.[27]

A 2017 systematic review of chastetree for premenstrual, postmenstrual and infertility disorders found it is widely used to treat PMS and PMDD (similar to PMS but more serious). In addition, it was shown to be beneficial in post-menstrual cases and it can also contribute to treatment of infertility cases in both men and women. "The plant contributes to improve many morbidities including [PMS], mastalgia, inflammation and sexual dysfunction, and also helps to relieve pain, and possesses antinociceptive effects. [Chastetree] is effective in reducing symptoms of many gynaecological problems. It is clinically used in abnormal uterine bleeding disorders... This plant is useful in mild hyperprolactinaemia and luteal phase defect..." [28]

An earlier systematic review evaluated the evidence for the efficacy and safety of chastetree extracts from randomised, controlled trials investigating women's health. Of the 12 trials included in the review eight investigated PMS, two PMDD and two latent hyperprolactinaemia. Seven of the eight trials found chastetree to be superior to placebo (five of six studies), pyridoxine (vitamin B6: one study) and magnesium oxide (one study). In PMDD one study reported chastetree to be equivalent to fluoxetine (an SSRI antidepressant known as Prozac). In latent hyperprolactinaemia one trial reported chastetree to be superior to placebo for reducing prolactin secretion stimulated by thyrotropin-releasing hormone (known to induce hyperprolactinaemia), normalising a shortened luteal phase (if it is shorter than 10 days it can be difficult to fall pregnant), increasing mid-luteal progesterone (may improve pregnancy and live birth rates) and 17β-oestradiol levels, while the other found chastetree comparable to bromocriptine (a dopamine receptor agonist used to treat hyperprolactinaemia) for reducing serum prolactin levels and improving cyclic breast pain.[29]

A randomised, placebo-controlled, double-blind study reported a reduction in a large portion of the PMS scores in two groups with the chastetree group being more significant. In the study 128 women who suffered from PMS were evaluated (active 62, placebo 66). All patients answered a self-assessment questionnaire about headache, anger, irritability, depression, breast fullness and bloating during the premenstrual period before the study. Forty drops of chastetree extract, or matching placebo, was administrated for six days before menstruation for six consecutive cycles.

Patients answered the self-assessment questionnaires again after six menstrual cycles. There was a significant difference in the rank of variables, in favour of chastetree, before and after the study. The researchers concluded that chastetree can be considered as an effective and well tolerated treatment for the relief of symptoms of mild and moderate PMS.[30]

The largest multicentre trial of chastetree for PMS was on 170 women. In the randomised, double-blind, placebo-controlled, parallel group comparison 86 women received 20mg a day (around 180mg dried herb) of chastetree and 84 received placebo for three menstrual cycles. Self-assessment of typical PMS symptoms resulted in significantly lower than average scores for the chastetree group by the end of the trial.[31]

According to the available evidence chastetree, when treating PMS, is more effective than pyridoxine treatment and has a similar response rate to fluoxetine, as noted above.[32,33]

In an open study without controls 93% of 1634 patients with PMS reported a decrease in, or cessation of, symptoms of PMS from using chastetree over a period of three menstrual cycles.[34]

Infertility and Menstrual Cycle Irregularities Activity

There is good evidence to support the use of chastetree to enhance female fertility. As anovulatory cycles, hyperprolactinaemia and hypothalamic dysfunction may all have a detrimental effect on fertility chastetree, which has demonstrated effects of lowering prolactin as well as regulating the HPO axis, and promotes a regular menstrual cycle, would appear useful.[35]

Chastetree is used to treat endometriosis with clinical trials supporting its use for infertility initiated by luteal phase dysfunction. It is widely used in endometriosis for its ability to regulate hormonal balance and improve the oestrogen-to-progesterone ratio, an imbalance that is implicated. Studies have shown that clinical pregnancy rates in those treated with chastetree were higher than that of the control group. As infertility affects 30 to 50% of women with endometriosis chastetree may be an effective treatment for endometriosis-related infertility.[36,37]

A placebo-controlled trial found chastetree treatment (equivalent to 20mg/day of dried fruit for three months) reduced prolactin release, normalised shortened luteal phases and corrected luteal phase progesterone deficiencies. Two women receiving the herb became pregnant.[38]

Other Activity

For veterinary herbalists there was an open trial involving 25 horses and ponies diagnosed with Cushing's disease (hyperadrenocorticism) where chastetree was administered for three months to animals that should have shed their coat (excessive hair growth). The study demonstrated reduced hirsutism which gave a healthier, shiner coat, with subsequent reduction in excessive sweating, improved energy levels and mood, apparent reduction in the incidence of laminitis (inflammation of the laminae of the foot – also known as founder), reduced excessive urination volume and extreme thirstiness and decreased abnormal fat deposits.[39]

Although chastetree is commonly used for hormonal and menstrual irregularities it may exert a novel melatoninergic activity. To date no human clinical trials exist testing chastetree in insomnia however a study of 20 healthy human males (aged 20 to 32) demonstrated a significant dose dependent increase of melatonin secretion using 120mg, 240mg and 480mg of the extract per day, compared with placebo, for 14 days.[40]

A recent pilot trial using chastetree for restless legs syndrome showed promising results. The researchers said dopamine agonists are first line therapy for restless legs syndrome. In a small group of 12 patients suffering from restless legs syndrome a standardised chastetree extract (40mg a day equivalent to 360mg dried herb) was tested as a dopamine agonist. Of seven patients receiving chastetree alone, five responded positively. Another five with more severe symptoms received chastetree with conventional dopaminergic agents, with four responding favourably by being able to reduce their drugs. One patient was able to cease pramipexol altogether.[41]

Indications

- Menstrual disorders including:
  - irregularities of the menstrual cycle including menorrhagia (heavy menstrual bleeding), altered menstrual cycle lengths or complete absence of ovulation and menstruation
  - infertility
  - habitual miscarriage associated with corpus luteum defect or low progesterone resulting from luteal phase defect
  - symptoms of premenstrual syndrome including congestive dysmenorrhoea, constipation, fluid retention, irritability, mood swings, breast pain, headaches and migraines and/or menopause including hot flushes
  - hormonally induced acne (in both sexes)
  - cyclical breast pain and benign breast disorders
  - ovarian cysts

  - fibroids
  - endometriosis
  - latent hyperprolactinaemia, a syndrome characterised by lower than normal progesterone secretion and normal to mildly elevated prolactin levels
  - PCOS, although this is contentious
- To help re-establish the cycle after use of the contraceptive pill
- To aid the expulsion of the placenta after birth
- Postnatal depression
- Fibromyalgia (due to modulating the HPO axis, its dopaminergic action, its cycle regulating activity and mood elevating properties)
- Hypothyroidism (due to hormone regulating activity)
- Restless leg syndrome
- Sleep maintenance insomnia
- Lactation support (low doses only - less than 150mg/day) as this is recently questioned due to the potential inhibition of prolactin – see contraindications)[42]

Energetics

Cooling and warming potential, dry, neutral.[43]

Use in Pregnancy

Chastetree is not traditionally recommended in pregnancy. In practice some herbalists use it during the first 10 weeks of pregnancy in cases of difficult conception. Current research suggests that "it is plausible that [chastetree] use during pregnancy (especially the second half) may negatively impact on the functional breast development that occurs in part in response to high circulating prolactin".[44,45]

Contraindications

People with tumours sensitive to oestrogen or progesterone should avoid using this herb until safety can be established. It has been suggested that the ability of chastetree to reduce prolactin levels may inhibit medical investigations and may mask diagnosis and proper treatment of prolactinoma.[46]

Use moderately during breastfeeding. Despite chastetree being recommended traditionally to promote breast milk the 2020 textbook *Advanced Clinical Naturopathic Medicine*, by Leah Hechtman, says there is sufficient data to indicate that chastetree has the potential to negatively impact lactation during its early months. It may also prompt an earlier return of menses which may deprive women of some of the health benefits associated with the lower levels of circulating oestrogen during lactation. "It would appear to be prudent to avoid this herb in women with low [breast milk] supply, and particularly during early lactation." "While there are some mixed findings with regards to the effect of [chastetree] on prolactin, the evidence overall suggests that [chastetree] may suppress prolactin. Suppression of prolactin and progesterone promotion are likely to have a negative effect on breast milk production in early lactation and are unlikely to assist with low supply in established lactation," Hechtman says.[47]

If the length of the menstrual cycle is excessively changed chastetree should be discontinued or the dose reduced.[48]

Drug Interactions

Observe patients. There are speculative, theoretical and hypothetical interactions for chastetree, based on *in vitro* evidence (cannot be extrapolated to human use), suggesting that it may bind oestrogen and dopamine receptors but these are not based on controlled studies. Combined use with certain medicines, including oral contraceptives pills (OCP), hormone replacement therapy and other medicines with hormonal and/or dopaminergic actions such as dopamine receptor antagonists (including antipsychotic drugs) and metoclopramide (for stomach and oesophageal problems including heartburn), may result in decreased efficacy or additive effects although there is limited evidence to verify the extent of these effects. Several clinical studies involving women taking oral contraceptives have confirmed the herb still reduces PMS symptoms and does not affect OCPs.[49,50]

On 2 May 2019, the Australian Therapeutic Goods Administration (TGA) had received one report of an unintended pregnancy following concurrent use of chastetree and levonorgestrel, a progesterone-only

oral contraceptive pill. One other similar case had also been reported internationally. They said there are limited studies into the interactions between chastetree and oral contraceptives. However, the potential for such an interaction is recognised internationally. "Health Canada and the European Medicines Agency advise consumers to consult a health practitioner prior to using [chastetree] - containing products if they are taking hormone-containing medications such as progesterone preparations, oral contraceptives or hormone replacement therapy, they said."
"Consumers taking an oral contraceptive to prevent pregnancy should be aware that [chastetree] may interfere with how well the contraceptive works. Consumers taking medicines with contraceptive, hormonal and/or dopaminergic actions should consult their health professional prior to combined use with [chastetree]." [51]

Administration and Dosage

Liquid Extract:	1:1
Alcohol:	45%
Weekly Dosage:[52]	5 to 20mL

Ruth Trickey says "it requires a lot of skill and knowledge to get the dose and timing right." She recommends it should be started as close as possible to day one of the menstrual cycle (preferably prior to ovulation) and continued throughout the whole cycle including the period. She says a three month course is usually necessary and some women may need longer courses to regulate ovulatory patterns. "For full benefit [chastetree] is usually prescribed for between three and nine months. Longer-term administration is necessary in some cases and there are reports of women taking chastetree for up to sixteen years without ill-effect. Positive changes to the menstrual cycle are usually evident in the first month; however, some women report longer or shorter cycles than usual initially, until stabilisation occurs," she says. "[It] is usually given as a single morning dose of 2ml of fluid extract". This is because it is considered that hormonal regulation via the pituitary is more receptive to this regime however there is no pharmacological or clinical evidence to support this. Trickey says dosage is important. Doses which are too high or too low may worsen some conditions, and should be adjusted according to the problem treated, any additional symptoms, and the age of the woman." She also suggests it should be prescribed cautiously (and only by a practitioner) for young women (under 20) "for whom the hypothalamic-pituitary-ovarian interplay is still fragile and easily disrupted." [53,54]

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