

## *CHASTEBERRY (VİTEX AGNUS CASTUS) AND PROLACTİNE*

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### Özet

Vitex agnus castus eski çağlardan beri kadınlar için ilaç olarak kullanılmıştır. Öncelikli olarak kadın hormonlarının üretimini düzenleyen bileşiklerin varlığı araştırılmalıdır. Vitex agnus castus prolaktin salınımını düzenler. Bu özellik infertilite tedavisinde yüksek düzeylerinin prolaktin seviyesinin azaltılmasına yaramaktadır.

**Anahtar Kelimeler:** Hayıt Meyvesi, Vitex agnus castus, Prolaktin.

### Abstract

Vitex agnus castus has been used since ancient times as a female remedy. Preliminary investigations do indeed show the presence of compounds which are able to adjust the production of female hormones. Vitex agnus castus may also regulate prolactin secretion. The ability to decrease excessive prolactin levels may benefit infertile women.

**Keywords:**Chasteberry, Vitex agnus castus, Prolactine.

### Introduction

Vitex agnus castus, also known as chastetree berry, chasteberry, monk's pepper, or simply vitex, is a fertility-promoting herb that is useful in treating hormonal imbalances. Vitex does indeed exert a normalizing effect on the monthly cycle, as well as balance the hormones involved in ovulation and menstrual regularity. Better yet, vitex (Figure1) (1) also appears to increase the odds of pregnancy.

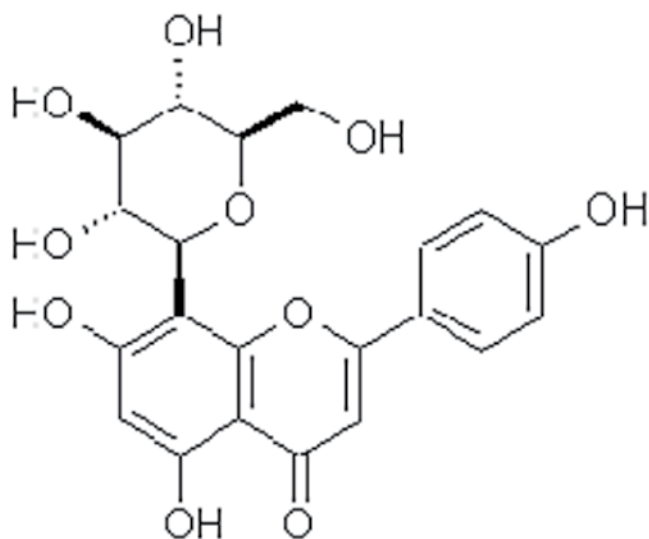
The fruits of Vitex agnus castus (the chaste tree) contain a mixture of iridoids and flavonoids, and some compounds similar in structure to the sex hormones have been isolated from the leaves and flowers. The effects of agnus castus have been described as similar to those of the corpus luteum.

Studies have shown that extracts of Agnus castus can stimulate the release of Lutenizing Hormone (LH) and inhibit the release of Follicle Stimulating Hormone (FSH). This suggests that the volatile oil has a progesterone-like effect. Its benefits stem from its actions upon the pituitary gland specifically on the production of luteinizing hormone. This increases progesterone production and helps regulate a woman's cycle.



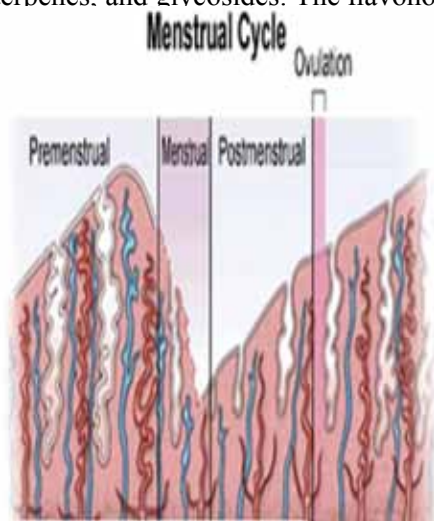
**Figure 1.:** Vitex agnus castus (httpI).

Extracts of the fruits of chaste tree *Vitex agnus castus* are widely used to treat premenstrual symptoms. Double-blind placebo-controlled studies indicate that one of the most common premenstrual symptoms, i.e. premenstrual mastodynia (mastalgia) is beneficially influenced by an chasteberry extract (2).



**Figure II:** Vitexin

Chasteberry isolates contain flavonoids, essential oils, diterpenes, and glycosides. The flavonoids (casticin,



**Figure III:** Menstrual cycle (<http> 2).

quer-cetagenin, isovitexin (Figure I)) have been shown in vitro to affect estrogen receptors. The mechanism of action is not exactly understood but it is assumed that it has dopaminergic effects resulting in changes of prolactin secretion.

Vitex' precise mechanism of action and its active constituents have not been established. Some constituents may have anti-inflammatory, sedative, and analgesic prop-

erties. Vitex also has dopaminergic properties, although it remains unclear which active compound is responsible.

### The mechanism of action

The mechanism of action may also be related to modulation of stress induced prolactin secretion via dopamine, without directly affecting luteinising hormone or follicle stimulating hormone (FSH).

Vitex both stimulates and regulates the key reproductive hormones involved in ovulation and assists in restoring balance and menstrual regularity (Figure II) (3).

Vitex agnus castus works by acting on the pituitary gland and the hypothalamus, which are responsible for releasing hormones or triggering hormone responses throughout the reproductive system. In vitro studies describe dopaminergic effects of vitex via a dose-dependent binding of dopamine-2 receptors, yielding potent inhibition of prolactin in cultured pituitary cells. The flavonoid apigenin can be isolated from vitex and has selective binding affinity for the beta-estrogen receptor subtype. Functional disorders of the menstrual cycle are typically interpreted as signs of hormonal imbalance, with estrogen dominance and progesterone deficiency during the luteal phase usually implicated, in addition to hyperprolactinemia. Chasteberry contains a variety of active compounds that affect different aspects of the reproductive system and create a balancing, or normalizing, effect. Some of these active compounds include essential oils, iridoid glycosides (agnuside and aucubin), and flavonoids (casticin and iso-orientin) (4).

The search for the chemical identity of the dopaminergic compounds resulted in isolation of a number of diterpenes of which some clerodadienols were most important for the prolactin-suppressive effects (5). They were almost identical in their prolactin-suppressive properties than dopamine itself. Hence, it is concluded that dopaminergic compounds present in *Vitex agnus castus* are clinically the important compounds which improve premenstrual mastodynia and possibly also other symptoms of the premenstrual syndrome Both extracts from *Vitex agnus castus* as well as synthetic dopamine agonists (Lisuride) significantly inhibit basal as well as TRH-stimulated prolactin secretion of rat pituitary cells in vitro and as a consequence inhibition of prolactin secretion could be blocked by adding a dopamine receptor blocker. Therefore because of its dopaminergic effect *Agnus castus* could be considered as an efficient alternative phytotherapeutic drug in the treatment of slight hyperprolactinaemia (6,7).

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In a pilot study, 56 women with mastodynia who took a product containing chasteberry for three menstrual cycles had significantly reduced serum prolactin levels compared to those taking placebo (10).

## Conclusion

Clinical studies in patients with premenstrual syndrome, luteal insufficiency, and mastopathy show a simultaneous decrease in the clinical syndrome score and prolactin levels (8).

A decrease of prolactin will influence levels of Follicle-stimulating hormone (FSH) and estrogen in women; and testosterone in men. Dopaminergic compounds (diterpenes with prolactin-suppressive effects that were almost identical in their prolactin-suppressive properties than dopamine itself) present in *Vitex agnus castus* seem likely to be the clinically important compounds which improve premenstrual mastodynia and possibly also psychic and somatic symptoms of PMS. *Vitex* did not modulate follicle stimulating hormone (FSH) or luteinizing hormone (LH) production in rat pituitary cells (11).

Initial human studies reported inhibition of FSH and stimulation of LH secretion and presumed the hormone modulation of FSH and LH affected the downstream hormones progesterone and estrogen (12).

*Vitex agnus castus* fruit extract has an anti-androgenic effect and probably acts through the Hypothalamic-Pituitary- Gonadal (HPG) axis (13).

Linoleic acid also stimulated mRNA ER $\beta$  expression in T47D:A18 cells, PR expression in Ishikawa cells, but not AP activity in Ishikawa cells. These data suggest that linoleic acid from the fruits of *Vitex agnus-castus* can bind to estrogen receptors and induce certain estrogen inducible genes (14).

In vitro studies provide evidence of prolactin inhibition with direct binding to dopamine receptors. Extracts were also demonstrated to displace ligands in human opioid-receptor binding (15).

Clinical reviews are available for the efficacy of vitex in hyperprolactinaemia, but so far no systematic review has been published on adverse events or drug interactions associated with *Vitex agnus-castus*. Therefore, this review was conducted to evaluate all the available human safety data of vitex monoprparations. Its dominant pharmacological effect on the body is inhibition of prolactin secretion. *V. agnuscastus* is available in a variety of dosage forms. Because of its dopaminergic effect *Agnus castus* could be considered as an efficient alternative phytotherapeutic drug in the treatment of slight hyperprolactinaemia.

There are no clinical studies assessing the safety of vitex in children and pregnant women. *Vitex* is generally not recommended in pregnancy due to its unknown effects on the pituitary.

It is concluded that dopaminergic compounds present in *Vitex agnus castus* are clinically the important compounds which improve premenstrual mastodynia and possibly also other symptoms of the premenstrual syndrome.

The influence of vitex extract is dependent on the dosage and the initial level of the prolactin concentration.

The result is a shift in the ratio of estrogen to progesterone, in favor of progesterone. The ability of chasteberry to raise progesterone levels in the body is an indirect effect, so the herb itself is not a hormone.

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