Vitex agnus castus and Some Female Disorders: A Review

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ABSTRACT

Vitex agnus castus L. is a deciduous tree which has been utilized in ancient Greece, Iran, Egypt and Rome for over 2500 years for a large variety of female reproductive system health difficulties. In Saudi Arabia, many women have menstrual cycle disturbances and menopausal dysfunction and many have polycystic ovary syndrome at young age. Using Vitex is not in Saudi tradition like other Arab countries. Recently, just few people used this herb for treating some infertility problems. A variety of beneficial effects of this curative herb have been reported in clinical studies, including antioxidant, anti-inflammatory, hypolipidemic, anti-diabetic, hormonal modulatory, anti-nociceptive and opioidergic activities, preventing oxidative stress and nonalcoholic fat liver disease. Adverse effects of the plant are mild and reversible. The advantages of this herb as natural medicine attract the people and make it one of best choose and utilize widely in women disorders especially that related with menopauses. Its constituents could interact with dopaminergic antagonists and exhibited progesterone and estrogenic activities. This brief review introduces this plant to Saudi society and others to expand it usage and discusses the potential effect of the plant to cure some of the women disorders displaying its main ingredients and the side effects.

Key words: Amenorrhea, Medicinal plant, Menopause, Vitex agnus-castus.

Natural sources and plants frame the promise of today's advanced pharmaceutical and contribute to a large scope to the commercial medicate productions fabricated nowadays. Almost 25% of drugs endorsed around the world are inferred from plants. Herbs still frequently used instead of drug in health cares (Wachtel-Galor et al., 2011). Over the past three decades, the use of herbal medicine has augmented significantly and at least 80% of people around the world depend on them for some part of primary healthcare (Ekor, 2014). Herbal remedies have also been widely used in many developed countries and becoming mainstream in the UK and the rest of Europe, as well as in North America and Australia (Anquez-Traxler, 2011). Based on the long history of using herbal perpetration on clinical issues of various indigenous societies, the success rate of creating new drug from natural herbal sources must be higher that from chemical perpetration (Pan et al., 2013).

Vitex agnus castus (VAC) is one of the herbs used as a medicinal plant. It is considered a traditional herbal remedy, primarily used in Anglo-American and European practice for a variety of female reproductive dysfunction (Van Die et al., 2013). It is derived from dried fruit of chastisea trees and since ancient Greece used as female boitincal health (Wuttke et al., 2003). In Morocco, vitex agnus is regularly utilized in conventional medication for treatment of many medical situations such as diabetes, rheumatism, respiratory, stomach related tract, dermatological, genitourinary and glands disorders (Berrani et al., 2018).

Vitex is often used to relieve the symptoms associated with female hormonal in-balances such as the depression, cramps, mood swings, water retention and weight gain. In European Medical practice and Herbalism, the Vitex recommended for uterine fibroid cysts and to assist alleviating the obnoxious side effects of menopause (Hobbs et al., 2005).

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Vitex agnus castus L. is a little deciduous chaste tree that has been employed in ancient Egypt, Iran, Greece and Rome for various gynecological issues over 2500 years (Niroumand et al., 2018). A variety of plant phytochemical including flavonoids and linoleic acid which may be responsible for the biological activities have been isolated from chasteberry (Chen et al., 2011; Webster et al., 2011).

In Saudi Arabia, many women have menstrual cycle disturbances and menopausal dysfunction and many have polycystic ovary syndrome at young age. Guraya, (2013), reported that many Saudi women have reproductive system problems such as PCOS in young age, delay in pregnancy, menstrual irregularity. Using Vitex is not common in Saudi tradition like other Arab countries. Recently, just few people used this herb for treating some infertility problems. So, this brief review to expand the use this herb and discuss the
different usages, beneficial effects of this medicinal plant and touching on the side effects.

The literature published from (1990-2019) was reviewed using the database google scholar, PubMed, research gate and Academia. The research was carried out using various terms such as *Vitex angus castus*, polycystic ovarian syndrome (PCOS), hormonal anomalies in female, menopause, the management of PCOS and management of menopause. All recovered articles were wisely evaluated and data were gotten.

**Characteristics of plants**

*Vitex angus castus* is a small tree that included in the family of Verbenaceae (Ono et al., 2011; Rani and Sharma, 2013; Rashed., 2013). The plant *Vitex angus castus* is a deciduous shrub that reaches a height of up to 5 m (Berrani et al., 2018). The leaves appear like fingers with 5-7 finger-like leaflets and 7.5-10 cm in diameter (Fig 1) (Niroumand et al., 2018). The leaves are arranged in opposite, with a lengthened petiole. The green leaflets are linear, lanceolate, toothed and dark on the top and grey below (Ono et al., 2011). The flowers are fragrant with lilac, blue, pink, or white color (Berrani et al., 2018). Fruits are berries which contains four seeds resemble to black pepper (Niroumand et al., 2018). The skin of the fruits is hard and has a purple to a black color, yellowish inside and half covered by their green sage-calyces. It has aromatic and spicy scent and the flavor is warm and singular after maturation (Berrani et al., 2018). This plant is viewed as one of a medicinal herbs because both the fruit berry and the dried leaves have been utilized in many therapeutic issues (Mancho and Edwards, 2005; Niroumand et al., 2018).

**Botany and Natural Occurrence**

*Vitex angus castus* is affiliated to Verbenaceae family, commonly known as chaste tree and monk’s pepper (Ono et al., 2011; Rani and Sharma, 2013). This tree grows in all Mediterranean regions, in tropical and subtropical regions (Rashed, 2013) and in temperate zone (Duymuş et al., 2014). VAC distributed not only the Mediterranean Region and Central Asia, but it also can be found in Southern Europe and cultivated in the various regions including the United States (Ono et al., 2011; Li et al., 2013; Rani and Sharma, 2013). The plant often found growing next to streams and it loves water, but it could be seen growing in dry, rocky spots on the Greek islands (Hobbs, 1991). VAC is growing in areas where the Mediterranean climate is dominant, rather rocky places, wetlands such as stream banks and valleys. VAC can also be found on limestone slopes, in sunny and warm areas (Rajić et al., 2016).

**Phytochemical compounds**

There are different reports on the Phytochemical continents of VAC. Fruits, flowers and leaves of VAC are reported to contain different bioactive compounds (Rajić et al., 2016). It includes Vitexlactam C, Vitexlactam B (Li et al., 2013), essential fatty acids, volatile oil, alkaloid, progestins, flavonoids, irido glycosides (Arokiyaraj et al., 2009), iridoids (Rajić et al., 2016), two simple phenols (Li et al., 2013), diterpenoids and phytosteroids which have antihistaminic, antioxidant anti-inflammatory, hepato-protective properties (El-Nawasany, 2019).

Irido glycosides are mainly two (agnuside, aucubin) (Li et al., 2013; Rajić et al., 2016). Flavonoids named as Casticin, luteolin7-methyl ether and luteolin 7-O-glucopyranoside (Aissaoui et al., 2016), vitexin, kaempferol, quercetagenin (Rajić et al., 2016), 5-hydroxy-3,6,7,42 -tetramethoxyflavone and artecutin (Li et al., 2013). Progestins includes progesterone, hydroxy progesterone and androstenedione (Rajić et al., 2016). Alkaloids such as viticin; volatile oil includes 1,8-cineole, limes, α-pinenes, β-pinenes. Essential fatty acids such as palmitic acid, oleic acid and stearic acid (Rajić et al., 2016). The two simple phenolic are p-hydroxybenzoic acid and p-hydroxybenzoic acid glucose ester (Li et al., 2013).

The main Chemical compounds of this plant include vitexin, casticin, agnuside, p- hydroxybenzoic acid, alkaloids, diterpenoids. Flavonoids, terpenoids, neolignans, one glyceride and phenolic compounds are found in its fruits (Rafieian-Kopaei and Movahedi, 2017).

**Traditional uses**

The use of VAC in medicine has a long history. Hippocrates (460-370 BC), The ophrastos (371-287 BC) and Pedanios Dioscorides (90-40 BC) already reported it on the preparation. It was used to inhibit libido, diseases of the uterus, promote wound healing and in the Middle Ages to preserve the vow of chastity so it was called chastity mud and chaste tree (Anwendung, 2009).

Since more than 2500 years, Vitex fruits have been linked to a number of gynecological issues in ancient Egypt, Greece, Iran and Rome. It was also used for its suspected libido suppression (Roemheld Hamm, 2005). It has long tradition in out dated medicine, as a medicinal plant. It has been commonly used since 17th century as a popular folk treatment for female reproductive dysfunction encompassing corpus luteum insufficiency, premenstrual syndrome (PMS), menopausal symptoms and inadequate milk production.
(Duymuş et al., 2014). It is used as diuretic, digestive anti- fungal, against anxiety and stomachache in Anatolian folk medicine (Kuruüzüm_Uz et al., 2003). It has been utilized for reproductive disorders in female since Greek and Roman times. In 4th century B.C., Hipocrates suggested the plant for treating injuries, inflammation and swelling of spleen. (Daniele et al., 2005).

During the past 50 years, chasteberry in Europe has been commonly used in premenstrual syndrome (PMS), menstrual bleeding, menstrual disorders and uterine dysfunction. The German commission E accepts the application of VAC by family doctors and gynecologists for menstrual cycle disorders, cyclic breast pain and PMS (Roemheld-Hamm, 2005).

Vitex fruits and leaves are ideal candidate as flavor and spice to be used in food and the berries as pepper alternative in Persian traditional medicine (Li et al., 2013). The fruits have been suggested as hormone-like medication to improve menstrual disorders and as antispasmodic, carminative, energizer, anticonvulsant, tranquilizer agents and to recover the digestive dysfunction (Ghanjadi et al., 2012). According to ethnomedicine of various nations, this shrub is utilized to relieve menstrual pain, spasmodic dysmenorrhea, insufficient lactation, treatment of acne and eyes disease, stomach pain, snake and scorpion bites and as antispasmodic, aphrodisiac and as emmenagogue agents (Niroomand et al., 2018). In folk medicine, it has been commonly used for treating insufficiency of ovaries, uterine bleeding, premenstrual syndrome, fibroid cysts, infertility and acne of teenagers. It has also historically been used to promote digestion, sedation and anti-infection (Arköyaraj et al., 2009).

The fruits of Vitex are called Manjingzi in Chinese Pharmacopoeia. Manjingzi is a Chinese traditional medicine used to recover ophthalmodynia, migraines and headaches. The leaves of Vitex are used in treating asthma, phlegm and coughs (Yao et al., 2016). Several parts of Vitex including seeds, roots and leaves are commonly used as anti-inflammatory, anti-rhumatism, analgesic and insecticide agents (Zheng et al., 2015).

In Arabic countries, the dried seed is taken orally as a lactogenic agent and emmenagogue. The hot water extract is used as a contraceptive and the entire plant is inhaled, by fumigation, as an emmenagogue (Razzack, 1980). In Morocco, the seed and leaf powder used externally or fumigation to treat burn, cold and headache (Saadi et al., 2013).

**Alternative and complementary medicine uses**

Nowadays, VAC is widely used in USA in complementary and alternative medicines as a medicinal plant to treat premenstrual syndrome (PMS) (Weis and Kaapen, 2009, Niroomand et al., 2018). It has fewer side effects so it used as effective alternative herbal medicine to treat symptom related to PMS (Röhrl et al., 2017). Fruits traditionally used to treat minor symptoms of PMS such as monthly pain, mood disorders and swelling (Dickerson, 2003; Röhrl et al., 2017). In Europe, the fruits extract used as effective alternative agent instead the chemical drugs to treat PSM (Berger et al., 2000). The agency of European medicines and Health authorities in Germany have confirmed the positive effects of the VAC on menstrual cycle management and the PMS and Mastalgia care (Girman et al., 2003 and Mari et al., 2015). It well known in North America and in Europe as an effective substitute instead of the pharmaceutical drugs in treating other different disorders such digestive complaints, Acne, infertility and lactation supports (Niroomand et al., 2018).

Vitex has been included in numbers of herbal perpetrations which used in clinical treatment. Clinical evidence indicates that the extract of VAC dried fruits is effective for the recovery of premenstrual syndrome, menstrual abnormality, amenorrhea, mastidynia and hyperprolactinaemia which all due to elevated the level of prolactin (Azarnia et al., 2007). Both fluid extract or dried leaves extract in pill form were used in clinical trials at various doses (Azarnia et al., 2007; Carmichael and Can, 2008; Dugoua et al., 2008). A routine consumption of 30-40 mg of dried herb in capsules or liquid preparation is recommended by German commission E monograph. This is normally taken once in the morning sequentially with liquid for several months. For premenstrual syndrome or heavy period, the herb can be consumed for 4-6 months on a regular basis. Infertile women with amenorrhea can consume the *V. agnus castus* for 12-18 months unless they are pregnant during treatment (Healthnotes Resource, 2006).

**Clinical application**

Chaste tree has dopaminergic, estrogenic, cytotoxic and probably antibiotic properties. Clinical studies have shown that it can be used to cure galactorrhea, mastodynia, hyperprolactinaemia and premenstrual syndrome. Sub-fertile women suffering from hormonal problems which resulted from hyperprolactinaemia with consecutive luteal phase insufficiency, using chaste tree preparation can be very helpful (Anwendung, 2009).

**Female reproductive system hormonal disorders**

The development and the function of the female reproductive system depends upon hormone concentrations and balance. Endocrine dysfunctions may lead to many abnormalities *e.g.*, menstrual cycle irregularities impaired fertilities endometriosis and polycystic ovarian syndrome (PCOS). These abnormalities may results from modulation of the concentration of estrogens thecal androgens and thyroid hormones (Nicopolou-Stamati and Pitsos, 2001). Irregular or absent menstrual periods due to ovulation problem which account for subfertility in 20-25% of couples It can be, substantiated through measurement of reproductive hormones (Bretveld et al., 2006).

Vitex modulates the rise or reduction in sex hormones by physiological and pharmacological activities (Liu et al., 2004). Studies by Jelodor and Askari (2012) demonstrated that the vitex extract rise the progesterone concentration and reduce the testosterone concentration but Vitex doesn’t change the level of de-hydro-epi-androstenedione
and estrogen in animal with polycystic ovary syndrome (PCOS). Ibrahim et al. (2008) found that Vitex rises the level of progesterone and estrogen hormone and decrease the level of LH without affecting FSH hormone in ovariectomized rats.

Vitex secrets substantial amount of androgen that converted to estrogen (Ibrahim et al., 2008). Apigenin is the main active phytoestrogen in vitex, can bind to the estrogen receptors (Jarry et al., 2003). Linoleic acid which considered one of estrogenic substance in Vitex, can binding to estrogen receptors and stimulate certain estrogen inducible genes (Liu et al., 2004). Vitex modulates the Luteal phase disorders in female and rises the progesterone level, thereby the chance of conception is improved (Ahangarpour et al., 2016). Lu et al. (2011) reported that Vitex probably elevates the progesterone concentration which leads to regulate luteal phase dysfunction.

Earlier research showed that VAC fruit extract controls the imbalance of sex hormone levels like progesterone hormone in PSM (Milewicz et al., 1993). Xu et al. (2014) revealed that Vitex returned the regular function of the abnormal estrous cycle in D-galactose and aging group female mice, Vitex, also lightly rise the weight of ovaries and uterus and ovaries and uterus weight / body weight percentage in D-galactose and aging group mice.

Primary dysmenorrhea

Many women monthly suffer from menstrual cramps which sever enough to impact their quality life and work productivity (Ju et al., 2014). In primary dysmenorrhea, a condition related to PMS, intense uterine contractions are thought to trigger moderate to intense pain and mediated by the release of prostaglandins, leukotrienes and infiltration of leukocytes that normally accompany the breakdown of endometrial lining (Röhrl et al., 2017). Primary dysmenorrhea identified by hyper-production of uterine prostaglandins, especially PGF2α and PGF 2 resulting in increased uterine tone and high-amplitude contractions (lacovides et al., 2015; Bernardi et al., 2017). Prostaglandin production is controlled by progesterone and progesterone level drops immediately prior to menstruation and progastandin level increase (Bernardi et al., 2017). It was found that Vitex extract modulate a number of potential mechanism responsible for dysmenorrhea. The studies on Vitex extract showed it is potent anti-inflammatory as it has ability to suppress leukotriene synthesis, cytokines release and reactive oxygen species (ROS) production from isolated leukocytes which prevent spasmodic action and support beneficial effects of extract (Röhrl et al., 2017).

Menopausal symptoms

Menopause is transition natural period occurs in women life (Noroz et al., 2010). Menopausal symptoms have significant undesirable effects on women quality life (Naseri et al., 2019). During menopause the activities of estrogen and progesterone dramatically reduced (Tanira et al., 2009). Taking VAC extract as a phytoestrogenic therapy can relieve menopausal symptoms in women (Naseri et al., 2019).

Conducting numerous alternative or complementary therapy to alleviate the unpleasant effects of menopause is commonly acceptable today. Amongst, phytoestrogens are conducted as hormonal remedies in menopausal women; which have less possible side effects due to their herbal source (Jing et al., 2009).

Vitex agnus-castus has phytoestrogenic activities (Ahangarpour et al., 2016) and used to cure irregular menstruation, menopausal complication and menstrual pain (Naseri et al., 2019). The dopaminergic activities of VAC are documented in pharmacological research, intimacy to opioid receptors and capability to rise melatonin secretion support the Vitex activities to reduce the menopausal symptoms (Van Die et al., 2009).

Furthermore Vitex agnus-castus has antiaging, antioxidant effects with high level of phytoestrogen. It was established that the Vitex decreases many aging problems in female mice reproductive system. It can be useful for some aging events such as oxidative stress, deficiency women’s sex hormones and an atrophic endometrium (Ahangarpour et al., 2016).

Adverse effects

The safety of VAC was studied and the adverse effects have been found to be mild and reversible (Bornhorst, 1996; dugoua et al., 2008; Ho Sh et al., 2011; Rani and Sharma 2013; Niroumand et al., 2018). The most common ones emphasize: Nausea, headache, mild gastrointestinal complaints, fatigue, Menorrhagia, dry mouth, acne, pruritus and erythematous rash (Rani and Sharma 2013; Daniele et al., 2005).

Randomized controlled trials conducted in a woman with PSM, luteal phase defects or premenstrual dysphoric disorder. Some of these studies did not mention any adverse effects and showed few adverse effects which included acne, multiple abscesses, inter-menstrual bleeding, urticarial and each event was reported once only and resolved without discontinuation. Non-randomized clinical trials conducted in women and men treated with VAC at least for 3 months, no mention of adverse events was made (Claudia et al., 2005).

CONCLUSION

Vitex agnus castus has long history as therapeutically herb and considered one of the most beneficial medicinal herbs, especially for women. It reduces symptoms of premenstrual syndrome, decreases prolactin hormone and helps to regulate reproductive hormones in women. It also relieves menopausal symptoms, improves the bad impact of menopause and improves fertility in women. Side effects are mild and reversible, so many studies have proven its safety and the usefulness of this plant.

REFERENCES

Ahangarpour, A., Najimi, S.A. and Farbod, Y. (2016). Effects of Vitex agnus-castus fruit on sex hormones and antioxidant indices in a d-galactose-induced aging female mouse model. Journal of the Chinese Medical Association. 79(11): 589-596.
Vitex agnus castus and Some Female Disorders: A Review

Aissaoui, H., Algrab, M. and Mezhoud, S. (2016). Chemical constituents of Vitex agnus-castus (Verbenaceae). Pharma Chemica. 8: 491-4.

Anquez-Traxler, C. (2011). The legal and regulatory framework of herbal medicinal products in the European Union: a focus on the traditional herbal medicines category. Drug Inf. J. 45: 15-23.

Anwendung, K. (2009). Vitex agnus castus. Gynäkologische Endokrinologie. 7: 33-38 DOI 10.1007/s10304-008-0285-2.

Arköiyaraj, S., Perinbam, K., Agastian, P. and Kumar, R.M. (2009). Phytochemical analysis and antibacterial activity of Vitex agnus-castus. International Journal of Green Pharmacy (IJGP). 3(2): 162-164.

Azarnia, M., Ejttemai-Mehr, S., Shakoor, A. and Ansari, A. (2007). Effects of Vitex agnus-castus on mice fetus development. Acta Med Iran. 45: 264-70.

Berger, D., Schaffner, W., Schrader, E., Meier, B. and Brattstrom, A. (2000). Efficacy of Vitex agnus castus L. extract Ze 440 in patients with pre-menstrual syndrome (PMS). Arch Gynecol. Obstet. 264(3): 150-3.

Bernardi, M., Lazzeri, L., Perelli, F., Reis, F.M. and Petragli, F. (2017). Dysmenorrhea and related disorders. F1000Research. 6: 1645. https://doi.org/10.12688/f1000research.11682.1.

Berrani, A., Lhoriht, L.A., Larbi, O.M., El Hessni, A., Zouari, M., Erahali, D. and Bengueddour, R. (2018). Hypoglycemic effect of Vitex agnus castus extract in diabetic rats induced by streptozotocin. Phytothérapie. 16(S1): S40-S47.

Bornhorst, H.L. (1996). Growing native Hawaiian plants: A how-to guide for the gardener. Honolulu: The Bess Press. 26-27.

Bretveld, R.W., Thomas, C.M., Scheepers, P.T., Zielhuis, G.A. and Roeleveld, N. (2006). Pesticide exposure: The hormonal function of the female reproductive system disrupted? Reproductive Biology and Endocrinology. 4(1): 30.

Carmichael, A.R. (2008). Can Vitex agnus castus be used for the treatment of mastalgia? What is the current evidence? Evid Based Complement Alternat. Med. 5: 247-50.

Chen, S.N., Friesen, J.B., Webster, D., Nikolic, D., van Breemen, R.B., Wang, Z.J., Fong, H.H., Farnsworth, N.R. and Pauli, G.F. (2011). Phytoconstituents from Vitex agnus-castus fruits. Fitoterapia. 82: 528-533.

Claudia, D., Coon, T. and Max, P.H. (2005). Vitex agnus castus: A Systematic Review of Adverse Events. Drug Safety. 28: 319-32.

Danielle, C., Coon, J.T., Pittler, M.H. and Ernst, E. (2005). Vitex agnus-castus. Drug safety. 28(4): 319-332.

Dickerson, L.M., Mazyck, P.J. and Hunter, M.H. (2003). Premenstrual syndrome. Am. Fam. Physician. 67(8): 1743-52.

Dugoua, J.J., Seely, D., Perri, D., Koren, G. and Mills, E. (2008). Safety and efficacy of chastetree (Vitex agnus-castus) during pregnancy and lactation. Can. J. Clin. Pharmacol. 15: e74-9.

Duymuş, H.G., Çiftçi, G.A., Yıldırım, Ş.U., Demirci, B. and Kmrm, N. (2014). The cytotoxic activity of Vitex agnus castus L. essential oils and their biochemical mechanisms. Industrial Crops and Products. 55: 33-42.

Ekor, M. (2014). The growing use of herbal medicines: issues relating to adverse reactions and challenges in monitoring safety. Frontiers in Pharmacology. 4: 177.

El-Nawasany, L.I. (2019). The use of Vitex Agnus-Castus to produce functional stirred yoghurt. J. of Food and Dairy Sci., Mansoura Univ. 10(9): 297-301.

Ghannadi, A., Bagherinejad, M., Abedi, D., Jalali, M., Absalan, B. and Sadeghi, N. (2012). Antibacterial activity and composition of essential oils from Pelargonium graveolens L'her and Vitex agnus-castus L. Iran J. Microbiol. 4: 171 6.

Girman, A., Lee, R. and Klgler, B. (2003). An integrative medicine approach to premenstrual syndrome. Am J. Obstet. Gynecol. 188: S56 65.

Guraya, S.S. (2013). Prevalence and ultrasound features of polycystic ovaries in young unmarried Saudi females. Journal of Microscopy and Ultrastructure. 1(1-2): 30-34.

Healthnotes Resource Page. Vitex agnus-castus. [Last accessed 2008 May 10]. Available from: http://www. healthnotes.com.

Ho, S.H., Singh, M., Holloway, A.C. and Crankshaw, D.J. (2011). The effects of commercial preparations of herbal supplements commonly used by women on the biotransformation of fluorogenic substrates by human cytochromes P450. Phytother Res. 25: 983 9.

Hobbs, C. (1991). The Chaste Tree: Vitex agnus-castus. Pharmacy in History. 33(1): 19-24.

Iacovides, S., Avidon, I. and Baker, F.C. (2015). What we know about primary dysmenorrhea today: a critical review. Human Reproduction Update. 21(6): 762-778.

Ibrahim, N., Shalaby, A., Farag, R., Elbaroty, G., Nofal, S. and Hassan, E. (2008). Gynecological efficacy and chemical investigation of Vitex agnus-castus fruits. Liby. J. Agr. Res. 5(1): 30.

Jarry, H., Spengler, B., Porzel, A., Schmidt, J., Wuttke, W. and Christoph, V. (2003) Evidence for estrogen receptor beta-selective activity of Vitex agnus-castus and isolated flavones. Planta Medica. 69: 945e67.

Jelodar, G. and Askari, K. (2012). Effect of Vitex agnus-castus fruits hydroalcoholic extract on sex hormones in rat with induced polycystic ovary syndrome (PCOS). Physiology and Pharmacology. 16: 62e69.

Jing, Z., Yang, X., Ismail, K.M., Chen, X. and Wu T. (2009). Chinese herbal medicine for premenstrual syndrome. Cochrane Database Syst. Rev. 21 (1): CD006414.

Ju, H., Jones, M. and Mishra, G. (2014). The prevalence and risk factors of dysmenorrhea. Epidemiologic Reviews. 36(1): 104-113.

Kuruuzum-Uz, A., Stroch, K., Demirezer, O. and Zeeck, A. (2003). Effects of Vitex agnus-castus fruits hydroalcoholic extract on sex hormones in rat with induced polycystic ovary syndrome (PCOS). Physiology and Pharmacology. 16: 62e69.

Kuruzuzum-Uz, A., Stroch, K., Demirezer, O. and Zeeck, A. (2003). Effects of Vitex agnus-castus fruits hydroalcoholic extract on sex hormones in rat with induced polycystic ovary syndrome (PCOS). Physiology and Pharmacology. 16: 62e69.

Li, S., Qiu, S., Yao, P., Sun, H., Fong, H.H. and Zhang, H. (2013). Components from the fruits of the popular European medicinal plant Vitex agnus-castus in chemoprevention via NADP (H): Quinone oxidoreductase type 1 induction. Evidence Based Complementary and Alternative Medicine. 2013: 432829, 7.

Liu, J., Burdette, J., Sun, Y., Deng, S., Schlett, S., et al. (2004). Isolation of lindolic acid as an estrogenic compound from the fruits of Vitex agnus castus L. (chaste-berry). Phytomedicine. 11: 18e23.
Vitex agnus castus and Some Female Disorders: A Review

Lu, A., Beehner, J. C., Czekala, N. M., Koenig, A., Larme, E. and Borries, C. (2011). Phytochemicals and reproductive function in wild female Phayre’s leaf monkeys (Trachypithecus phayrei crepusculeus). Hormones and Behavior. 59: 28e36.

Manh, P. and Edwards, O.T. (2005). Chaste tree for premenstrual syndrome. An evolving therapy in the United States. Advance for Nurse Practitioners. 13: 43-46.

Mari, A., Montoro, P., D’Urso, G., Macchia, M., Pizza, C. and Piccente, S. (2015) Metabolic profiling of Vitex agnus castus leaves, fruits and sprouts: Analysis by LC/ESI/(QqQ) MS and (HR) LC/ESI/(Orbitrap)/MS n. Journal of Pharmaceutical and Biomedical Analysis. 102: 215-21.

Milewicz, A., Gejdel, E., Sworen, H., Sienkiewicz, K., Jedrzejak, J., Teucher, T. and Schmitz, H. (1993). Vitex agnus castus extract in the treatment of luteal phase defects due to latent hyperprolactinemia. Results of a randomized placebo-controlled double-blind study. Arzneimittelforschung. 43: 75266.

Naseri, R., Farnia, V., Yazdchi, K., Alikhani, M., Basanj, B. and Salemi, S. (2019). Comparison of Vitex agnus-castus extracts with placebo in reducing menopausal symptoms: A randomized double-blind study. Korean Journal of Family Medicine. 40(6): 362-367. https://doi.org/10.4082/kjfm.18.0067.

Nicopolopoulou-Stamati, P. and Pilts, M.A. (2001). The impact of endocrine disrupters on the female reproductive system. Human, Reproduction. Update. 7(3): 323-330.

Niroumand, M.C., Heydarpour, F. and Farzaei, M.H. (2018). Pharmacological and therapeutic effects of Vitex agnus-castus L.: A review. Pharmacognosy Reviews. 12: 103-14.

Noroozi, A., Kashi, N. and Aslam, A. (2010). Attitudes and perceptions of women 45 years of menopause. Journal of Health Systems Research. 7:14.

Ono, M., Eguchi, K., Konoishi, M., Furusawa, C., Sakamoto, J., Yasuda, S., Ikeda, T., Okawa, M., Kinjo, J., Yoshimitsu, H. and Nohara, T. (2011). A new diterpenoid glucoside and two new diterpenoids from the fruit of Vitex agnus-castus. Chemical Pharmaceutical Bulletin (Tokyo). 59: 392-6.

Pan, S.Y., Zhou, S.F., Gao, S.H., Yu, Z.L., Zhang, S.F., Tang, M.K., Sun, J., Ma, D., Han, Y., Fong, W. and Ko, K. (2013). New perspectives on how to discover drugs from herbal medicines: CAM’s outstanding contribution to modern therapeutics. Evidence-Based Complementary and Alternative Medicine. 2013: 25.

Rafieian-Kopaei, M. and Movahedi, M. (2017). Systematic review of premenstrual, postmenstrual and infertility disorders of Vitex agnus castus. Electronic Physician. 9(1): 3685.

Rajić, M., Molnar, M., Bilic, M. and Jokić, S. (2016). The impact of extraction methods on isolation of pharmacologically active compounds from Vitex agnus-castus-a review. International Journal of Pharmaceutical Research and Allied Sciences. 5(4): 15-21.

Rani, A. and Sharma, A. (2013). The genus Vitex: A review. Pharmacognosy Reviews. 7(14): 188-192.

Rashed, K.N. (2013). Antioxidant activity of different extracts of Vitex agnus-castus (L.) and phytochemical profile. Research in Pharmacy. 3(6): 01-05.

Razzack, H.M.A. (1980). The concept of birth control in Unani medical literature. Unpublished Manuscript of the Author, 64 pp.

Roemheld Hamm, B. (2005). Chasteberry. American Family Physician. 72: 821 4.

Röhrl, J., Werz, O., Ammendola, A. and Künstle, G. (2017). Vitex agnus-castus dry extract BNO 1095 (Agnucaston®) inhibits uterine hyper-contractions and inflammation in experimental models for primary dysmenorrhea. Clinical Phytoscience. 2(1): 1-12.

Saadi, B., Msanda, F. and Boubaker, H. (2013). Contributions of folk medicine knowledge in Southwestern Morocco: the case of rural communities of Imouzzer Ida Outanane Region. International Journal of Medicinal Plant Research. 21(1): 135-145.

Tanira, S., Wazed, F., Sultana, A., Amin, R., Sultana, K. and Ahmad S. (2009). Knowledge, attitude and experience of menopause an urban based study in Bangladesh. Journal of Dhaka Medical College. 15: 39-6.

van Die, M.D., Burger, H.G., Teede, H.J. and Bone, K.M. (2009). Vitex agnus-castus (Chaste-Tree/Berry) in the treatment of menopause-related complaints. The Journal of Alternative and Complementary Medicine. 15(8): 853-862.

van Die, M.D., Burger, H.G., Teede, H.J. and Bone, K.M. (2013). Vitex agnus-castus extracts for female reproductive disorders: a systematic review of clinical trials. Pianta Medica. 79(07): 562-575.

Wachtel-Galor, S. and Benzie I.F.F. (2011). Herbal Medicine: An Introduction to Its History, Usage, Regulation, Current Trends and Research Needs. In: Herbal Medicine: Biomolecular and Clinical Aspects. [Benzie I.F.F., Wachtel-Galor S., (editors)]. 2nd edition. Boca Raton (FL): CRC Press/Taylor and Francis, Chapter 1. Available from: https://www.ncbi.nlm.nih.gov/books/NBK92773/.

Webster, D.E., He, Y., Chen, S.N., Pauli, G.F., Farnsworth, N.R. and Wang, Z.J. (2011). Opioidergic mechanisms underlying the actions of Vitex agnus-castus L. Biochemical Pharmacology. 81(1): 170-177.

Weisz, G. and Knapen, L. (2009). Diagnosing and treating premenstrual syndrome in five Western Nations. Social Science and Medicine. 68: 1498 505.

Wuttke, W., Jarry, H., Christoffel, V., Spengler, B. and Seidlová-Wuttke, D. (2003) Chaste tree (Vitex agnus-castus): pharmacology and clinical indications. Phytomedicine. 10: 348-357.

Xu, Y., Ding, J., Ma, X.P., Ma, Y.H., Liu, Z.Q. and Lin, N. (2014). Treatment with Panax ginseng antagonizes the estrogen decline in ovarioectomized mice. International Journal of Molecular Sciences. 15: 7827e40.

Yao, J. L., Fang, S. M., Liu, R., Oppong, M. B., Liu, E. W., Fan, G. W. and Zhang, H. (2016). A Review on the Terpenes from Genus Vitex. Molecules (Basel, Switzerland). 21(9): 1179. https://doi.org/10.3390/molecules21091179.

Zheng, C. J., Li, H. Q., Ren, S. C., Xu, C. L., Rahman, K., Qin, L. P. and Sun, Y. H. (2015). Phytochemical and pharmacological profile of Vitex negundo. Phytotherapy Research. 29(5): 633-647.