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Vitex agnus castus –An overview

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Abstract

Vitex agnus castus was already in ancient medicinal art as an official medicinal plant and is named in the work of Hippocrates, Dioskurides, Theophrastus and others. This review attempts to encompass the available literature on Vitex agnus castus with respect to its pharmacognostic characters, traditional uses, chemical constituents and summary of various pharmacological activities and clinical effects. Other aspects such as toxicology and precautions are also discussed.

Key words : Vitex agnus castus, pharmacology, chemistry, clinical applications.

1. Introduction

Medicinal plants, which form the backbone of traditional medicine, have in the last few decades been the subject for very intense pharmacological studies; this has been brought about by the acknowledgement of the value of medicinal plants as potential sources of new compounds of therapeutics value and as sources of lead compounds in the drug development. In developing countries, it is estimated that about 80% of the population rely on traditional medicine for their primary health care. There arises a need therefore to screen medicinal plants for bioactive compounds as a basis for further pharmacological studies.

The genus name Vitex [1] contains the oldest root "vei", which means "wind, bend, plait" and it characterizes the flexible, but tough and hard branches, which were used to manufacture woven fences. Plinius - first century AD - already called the plant Vitex likely as a deduction for vitilium (lat.) (= wickerwork) (Plinius secundus, 1892-1898). Previously Homer also knew the shrub and called it lygos (Greek) (= flexible branch). The specific name "agnus castus" originated from the Latin "castitas" (chastity) and the equalization of the Greek "agnos" with the Latin "agnus" (lamb). But in contrast to the Latin word, the Greek word "agnos" was derived from a = "un" and gonos = "offspring, progeny.

Vitex agnus-castus, the chaste tree is a beautiful little deciduous tree or large shrub with a showy summertime flower display [2] .The leaves are 3-4 in (7.6-10 cm) in diameter with 5 to 7

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fingerlike leaflets[3]. The chaste tree is a sprawling plant that grows 10-20 ft (3-6 m) and about as wide.[4] Branched flower clusters are produced on new wood in late spring and early summer in a great flush that makes the tree look like a hazy purple cloud .It continuous to bloom sporadically until early fall. The parts used today as herbal medicine are the dried ripe berries (Agni casti fructus).

Chaste tree is native to woodlands and dry areas of southern Europe and western Asia. Because of its many admirable attributes, the chaste tree is a garden favorite wherever in the world it can be grown.The plant prefers light (sandy) and medium (loamy) soils, requires well drained soil and can grow in nutritionally pure soil.[5] The plants prefers acid, neutral and basic (alkaline) soils. It cannot grow in the shade.

In the traditional system of medicine, the plant is used for various health problems and diseases. Therefore the aim of this paper is to present an overview of pharmacognostical, traditional, phytochemical and pharmacological investigation carried out on the plant.

2.Pharmacognostical Characteristics

2.1 Macroscopical

Chaste tree can be grown as a large, deciduous, multistemmed shrub or a small, 10 to 15 feet tall tree.[6] Leaves bluish-green, opposite, hand-shaped, composed of five to seven radiating Leaflets

which are borne on a main stalk; leaflets linear, entire, lanceolate, lance-shaped, toothed, dark green above and grey beneath with a very close felt [7] Flowers fragrant and blue, lilac, rose or white color[8]; berries peppercorns like, hard with a purple to black skin, yellowish within, half- covered by their sage-green calyces, containing four seeds [9]; odour aromatic, spicy; taste warm and peculiar.

2.2 Microscopical [10-13]

The powdered fruits ate dark-brown and contain pale pieces

The calyx is covered with monocellular to multicellular curved hairs.The fruit is divided into the thin, soft exterior exocarp and the thick, very hard, internal endocarp. Short pedunculated glandular hairs with tetracellular glandular capitules are located on the outside of the exocarp which contain the essential oil. The exocarp itself consists of thin-skinned, brown parenchymatic cells and thicker partly lignified cells with many spots. The endocarp occupies the main part of the fruit and consists oil brachyscleried cell nests. The small and fatty seeds have a thin septum with large parenchymatic cells, which have rubbed thickenings.The nutritive tissue and the cells of the germ contain aleuron grains Starch is absent.

2.3 Historical aspect and traditional use

The plant *Vitex agnus castus* has been used medicinally for atleast two thousand years.The Greek goddess Hera is said to have been born under an agnus castus shrub. The shrub was a symbol of chastity in those days.[14] Women of ancient Athens, who celebrated the thesmophory a festival for the goddess Demeter, adorned themselves with *Vitex agnus castus* flowers and spread the leaves on their couches to preserve chastity.[15] In the middle ages, Christian monks used the berries, which smell and taste like pepper, as a spice and as an anaphrodisiac, hence the derivation of the name monks pepper Dioscorides, a greek physician, mentioned it as a beverage taken to lower libido [16]. In actual clinical trials, the fruit Agni casti fructus was shown to relieve premenstrual syndrome[17] (PMS) including corpus luteum insufficiency, premenstrual syndrome (PMS), menopausal symptoms[18] and insufficient milk production and especially breast swelling and pain, due to

its dopaminergic effect[19]. Side effects are rare and include rash, GI disorders, headache and increased menstrual flow.

2.4 Phytochemical Properties

Vitex agnus castus contains iridoids, flavonoids, diterpenoids, progestins, essential oils and ketosteroids.[20] Total polyphenolic content for the leaves (7.36% to 20%), flowers (9% to 10.64%) and fruits (6.92% to 24%) has been determined. the highest tannin content was found in the leaves (0.68% to 3%); tannin content was similar in the flowers (0.24% to 2%) and fruits (0.24% to 1.6%). [21]

Iridoid glycosides have been isolated from the leaves and fruits of the plant and include agnoside (0.7% in leaves), aucubin [22] (0.3%) and unidentified glycosides constituted 0.07%. The methanolic extract of the flowering stems of Vitex agnus-castus yielded three new iridoids [23]: 60-O-foliamenthoylmussaenosidic acid (agnucastoside A), 60-O-(6,7-dihydrofoliamenthoyl) mussaenosidic acid (agnucastoside B) and 7-O-trans-p-coumaroyl-60-Otrans-caffeoyl-8-epiloganic acid (agnucastoside C)

The flavonoid content has been determined in chaste tree leaves (1.0-2.7%), flowers (1.0-1.5%) and fruits (0.5-1.0%). Flavonoids include flavonol derivatives of kaempferol, vitexin and quercetagetin, the major constituent being casticin. Four new flavonoids, luteolin *6-C-(4"-methyl-6"-O-trans-caffeoylglucoside),* luteolin 6-C-(6"-O*trans-caffeoylglucoside),* luteolin *6-C-(2"-O-trans-caffeoylglucoside)* and luteolin 7-O-(6"-p-benzoylglucoside[24].together with four known ones 5,4'-dihydroxy-3,6,7, Y-tetramethoxyflavone, luteolin, artemetin and isorhamnetin were isolated from the root bark of *Vitex agnus-castus*[25]

The Alkaloids viticin is present in the plant. From the fruits of *Vitex agnus castus*-L one new diterpene 6, 7, diacetoxy-13-hydroxy-labda -8,14-diene as well as two previously described diterpenes (rotundifuran and vitexilactone) were isolated[26]. All the diterpenoids belongs to labdane type.A novel labdane diterpene alkaloid, vitexlactam A was isolated as a prism from the *n*-hexane extract of the fruits of *Vitex agnus-castus* through normal and reverse phase column chromatography. [27,28]

Essential oils present in the chaste tree mainly includes the following: monoterpenoids, 1, 8-cineol, limes, linalool, terpinyl acetate, alpha pinenes and beta along with sabinene, castine, myrcene, citronellol, cymene and camphene. Sesquiterpenoids such as caryophyllene, farnescene, cardinene and ledol also are present. The berries contain 5% volatile oil [29,30]

Numerous Essential fatty acids such as palmitic acid, oleic acid, linoleic acid, stearic acid have also been isolated.

Although found in trace amounts progesterone, hydroxyprogesterone, testosterone, Epitestosterone, androstenedione have been isolated from the leaves and flowers of *Vitex agnus castus.* [31, 32]

2.5 Pharmacological and clinical Studies

Vitex agnus castus contains substances that competitively bind receptors, making the plant useful in disorders in which progesterone deficiency might be suspected. (i.e. female infertility, menopause, PMS)

2.6 Effects on Premenstural Mastodynia

Double blind placebo controlled studies indicate that one of the most common premenstrual symptoms is beneficially influenced by Agnus castus extract and numerous less rigidly controlled studies indicate that Agnus castus extract have also beneficial effects on other psychic and somatic symptoms of PMS[33] . Premenstural mastodynia is more likely due to

latent hyperprolactinemia.[34] and it is concluded that dopaminergic compounds present in *Vitex agnus castus* are clinically the important compound which improve premenstrual mastodynia (due to high prolactin secretion) and possibly also other symptoms of premenstrual syndrome[35]

2.7 Effects on Infertility

In a randomized, prospective, placebo controlled double blind study, 96 women with fertility disorders took the vitex preparation Mastodynon® (30 drops twice a day) or placebo for three months and the outcome measures were a) pregnancy, b) spontaneous menstruation in women with amenorrhea and/or subsequent pregnancy, or c) improved concentrations of luteal hormones, were achieved significantly more often in the Mastodynon group compared to the placebo group (57.6% versus 36.0%, p = 0.069). [36]

2.8 Effects on Premenstrual syndrome

Numerous case studies have noted an effect of vitex on premenstrual aggravations such as mouth ulcers, acne, and premenstrual edema A monograph on vitex noted a monitoring survey to study the effect of the liquid vitex extract Agnolyt® (40 drops Daily) in 1542 women with PMS, ages 13 to 62. Thirty-three percent of the patients reported total relief of their symptoms, and an additional 57% reported partial relief. In a multicenter controlled double blind study, women ages 18 to 45 with PMS took a vitex tincture (1:5, 175 mg/day) or pyridoxine (200 mg/day), the total symptom score decreased comparably in the two groups. [37]

2.9 Effects on Cyclic mastalgia

In an open study, 52 women with cyclic mastalgia took 30 drops of vitex extract twice a day for three months; most women reported disappearance or improvement of symptoms In a randomized, double blind, crossover, placebo-controlled study in 20 women with cyclic mastalgia, women who received three months of treatment with Mastodynon® (a vitex extract) had significant relief of symptoms compared to those who took placebo, In a double blind, placebo controlled study of 100 women with cyclic breast pain, 1.8 ml of vitex extract daily for three months reduced menstrual associated breast pain [38].

2.10 As a Lactagogue

In a healthy lactating rats, high doses of vitex reduced milk production significantly compared to controls.On the other hand,other animal studies have found an increase in lactation and mammary enlargement.

Two early studies found a favorable effect of vitex on milk production. A study found an increase in milk production in 80% of 125 patients in a 1957 controlled trial in 817 patients, there was a significant effect from vitex administration, with average milk production about three times that of controls after 20 days of treatment.[39]

2.11 Effects on Hyperprolactinemia and PMS

Chaste tree preparations inhibit basal and thyrotropin-releasing hormone (TRH)-stimulated prolactin secretion from rat pituitary cells in vitro, suggesting its possible use in the treatment of hyperprolactinemia. In addition, animal studies found an increase in lactation and mammary enlargement, indicating an effect on prolactin release.

In a placebo controlled crossover double-blind study of 20 healthy men, vitex had different effects on prolactin release at different concentrations. Men received doses of 120 mg, 240 mg or 480 mg of a special vitex extract daily for 14 days. There was a significant

increase in prolactin level in men receiving the lowest dose, but a slight reduction in prolactin level in those receiving the higher doses [40]. There were no significant dose-dependent changes in the 24-hour serum prolactin profile. The changes that occurred during the treatment period depended on the baseline prolactin levels of the individual subjects.

2.12 Antimicrobial: *[41-43]*

Vitex demonstrated antimicrobial activity against *Staphylococcus aureus, Streptococcus faecalis, Salmonella species, Escherichia coli* (10-20%), *Candida albicans, C. tropicalis, C. pseudotropicalis*, and *C. krusei* (10-40%). Vitex extracts inhibited the growth of the dermatophytes and molds species: *Trichophyton mentagrophytes, Epidermophyton floccosum, Microsporum canis* and *M. gypseum*.

3. **Skin and mucus membranes**

3.1 Acne

A few clinical studies have investigated vitex' use in the treatment of acne In a controlled trial of 161 acne patients, reported in a monograph on vitex, three months minimum treatment with vitex resulted in an improvement in 70% of patients, a result which was significantly better than placebo. [44]

3.2 Evidence of efficacy of vitex agnus castus

Preparations of Agnus Castus (AC) are used in several gynecological indications such as cyclical mastalgia, premenstrual syndrome (PMS) and cycle disorders. The most common cause of cycle disorders and cyclical mastalgia is a manifest or a latent elevated level of prolactin. Various experimental pharmacological studies have shown that Agnus Castus extract contains substances with dopaminergic effects via binding to the D_2-receptor, which inhibit the release of prolactin.In four out of seven clinical studies a significant decrease of initially elevated basal prolactin levels and significant effects on the clinical symptoms have been observed. [45]

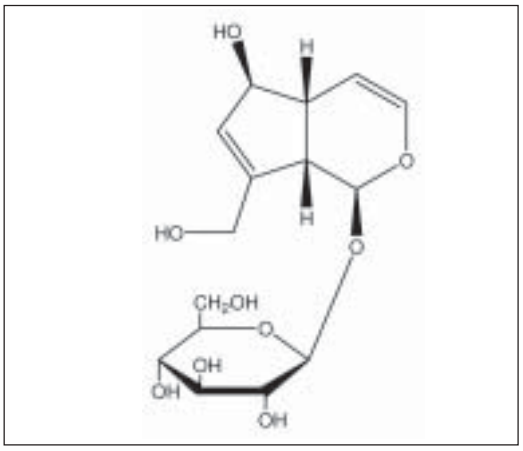

Fig. 1 (A): Aucubin

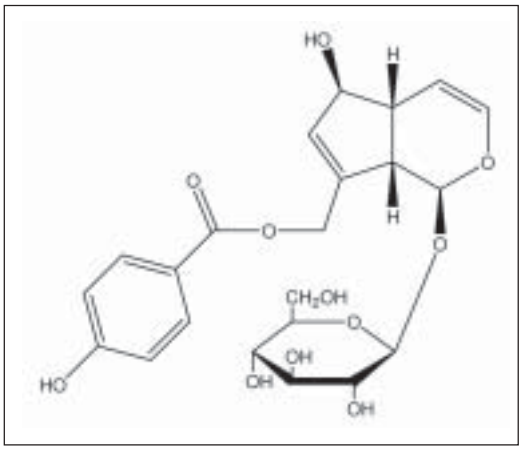

Fig. 1 (B): Agnuside

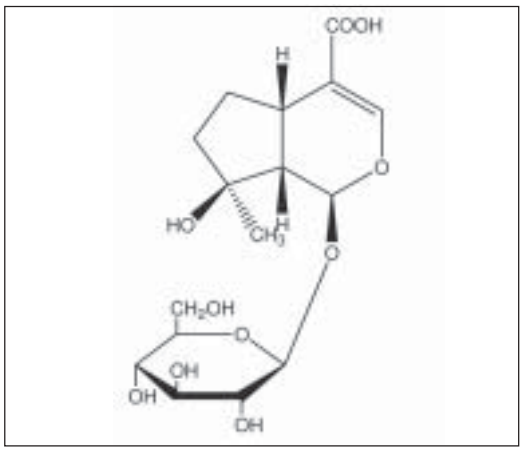

Fig. 1 (C): Mussaenosidic acid

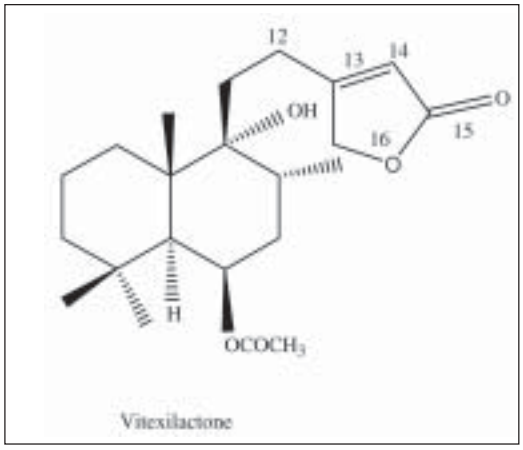

Fig. 1(D): 6'-o-p-hydroxybenzoylmussaenosidic acid

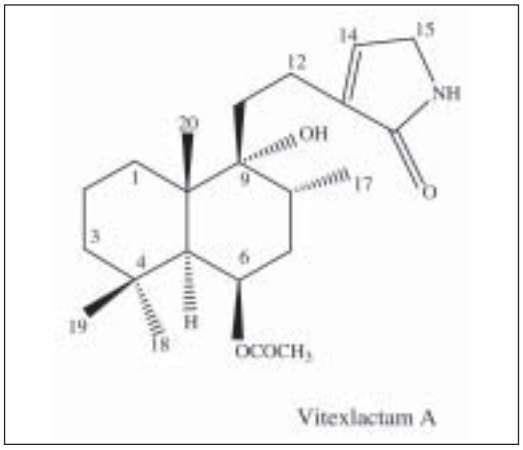

Fig. 1 (E): 6'-o-foliamenthoylmussaenosidic acid

4. Toxicity and Contraindications

4.1 Acute toxicity

Side effects are rare and may include itching, rash, headache, hair loss, fatigue, agitation, dry mouth, tachycardia, nausea and increased menstrual flow There is one case report of mild ovarian hyper stimulation in a woman who self-prescribed vitex

4.2 Allergic reactions to vitex have not been reportedInteractions with other herbs or pharmaceuticals

There are no reports of herb-drug interactions involving vitex. Some herbalists believe that vitex could interfere with birth control pills, hormone replacement therapy, and other hormone replacement medication, Additionally, it has been hypothesized that individuals taking drugs classified as Dopamine - receptor antagonists should use caution when taking vitex because

animal studies indicate that vitex may interfere with the dopamine receptor.[46]

4.3 Safety during pregnancy, lactation and/or childhood

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. There is insufficient information on the safety of using vitex during nursing. However, analysis for breast milk revealed no changes in composition.[47]

4.4 Availability of standardized preparations

Standardized preparations used in Europe include Agnolyt®; Strotan®; and Mastodynon®. Examples of standardized products available in the US include Chaste Tree Berry Extract from Enzymatic Therapy, standardized to 0.5% agnuside; Power Herbs Chasteberry Power from Nature's Herbs, standardized to a minimum of 0.9% glycosides and combined with dong quai and Siberian ginseng; and a Nutritional Dynamics product standardized to 0.5% agnuside and 0.6% aucubin.

5. Conclusion

In recent years ethno botanical and traditional uses received much attention as this brings to light the numerous little known and unknown medicinal virtues especially of plant origin which needs evaluation on modern scientific lines such as phytochemical investigation, biological evaluation on experimental animal models, toxicity studies, investigation of molecular mechanism of action of isolated phytoprinciples and their clinical trials. *Vitex agnus castus* possess various traditional uses and pharmacological activities as discussed in the present paper .However it is imperative that more clinical and pharmacological studies should be conducted to investigate the unexploited potential of this plant**.**

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