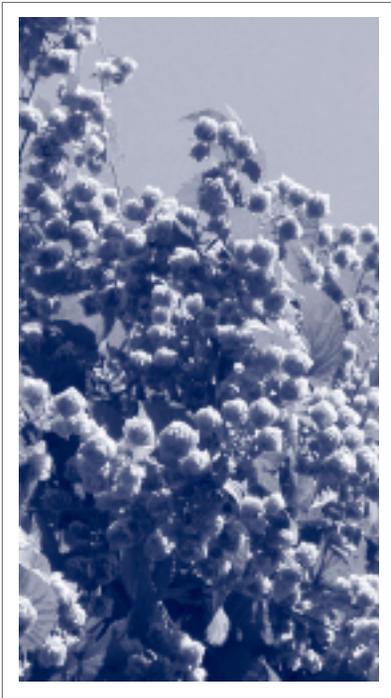


Humulus lupulus (Hops) Indiana photo



Humulus lupulus

Description

Humulus lupulus (hops) is a climbing perennial vine that vigorously grows 20-35 feet each year. *Humulus lupulus* is a member of the hemp family, which has grown wild since ancient times in Europe, Asia, and North America. The female flowers mature in late summer and are used to add bitterness, flavor, and aroma to beer. In ancient times the young shoots were eaten as a vegetable and the dried flowers were used for their slight narcotic effect and sedative action in the treatment of mania, toothache, earache, and neuralgia.¹ Modern herbal medicine practitioners continue to use hops as a sedative and mild hypnotic, as well as for its endocrine, free radical scavenging, and antitumor properties.

Active Constituents

The majority of hops' medicinal actions have been attributed to its flavonoid constituents. Flavonoids are composed of different chemical classes such as flavones, isoflavones, flavonols, flavanols, flavanones, and chalcones. These compounds differ in the level of oxidation of the flavane nucleus and in the number and position of hydroxyl, methyl, and methoxyl substituents.² Six chalcones (xanthohumol, 2',4',6',4-tetrahydroxy-3'-prenylchalcone, 2',4',6',4-tetrahydroxy-3'-geranylchalcone, 5'-prenylxanthohumol, dehydrocycloanthohumol, and dehydrocycloanthohumol hydrate) and three flavanones (isoxanthohumol, 6-prenylnaringenin and 8-prenylnaringenin) have been isolated from the hops plant.³

The endocrine properties of hops are due to the high estrogenic activity of the prenylated flavonoid 8-prenylnaringenin.⁴ Other prenylated flavonoids, including isoxanthohumol and xanthohumol, have exhibited high chemopreventive, antiproliferative, and cytotoxic effects in human cancer cell lines.^{5,6} Humulon, one of the bitter hop acids essential for brewing, has been used as an antibiotic and antifungal agent. The antimicrobial activity of humulon is used primarily for preserving beer.^{7,8}

Mechanism of Action

A mice study revealed the chemopreventive activity of hops flavonoids appears to be due to induction of quinone reductase (a hepatic phase II detoxifying enzyme) and reduced expression of CYP1A1 (a phase I enzyme that activates chemical carcinogens).⁹ Prenylated flavonoids from hops decreased growth and destroyed human breast, colon, and ovarian cancer cells *in vitro*.⁶ Hops flavonoids have also exhibited the ability to scavenge reactive nitrogen and oxygen species by inhibiting neuronal nitric oxide synthase and 3-morpholinonydnonimine-induced oxidation of LDL.¹⁰ The sedative and sleep-inducing activity of hops are poorly understood.

Evaluation of the estrogenic activity of hops showed significant competitive binding to estrogen receptors (ER-alpha and ER-beta), induction of alkaline phosphatase activity, up-regulation of progesterone receptor mRNA in cultured endometrial cells, and up-regulation of preselin-2, another estrogen-inducible gene.¹¹

Clinical Indications

Female Endocrine Disturbances

Common menstrual disturbances among female hops-pickers suggest a potential endocrine effect of the hops plant. In Germany, hops baths were used to treat gynecologic disorders and hops extracts have been reported to reduce hot flashes in menopausal women.¹²

Results from *in vitro* assays for estrogen activity suggest potential use for hops as a dietary supplement in the treatment of menopausal symptoms, although animal and human studies are currently lacking. *In vitro* investigation of active constituents showed that 8-prenylnaringenin alone competed the strongest against 17 β -estradiol for binding to both alpha- and beta-estrogen receptors.⁴ It also has been suggested that 8-prenylnaringenin has activity equal to or greater than other established plant estrogens.¹³ Isoflavonoid phytoestrogens have been associated with a reduction in incidence of breast and prostate cancer, cardiovascular disease, and menopausal symptoms.^{14,15}

Nervousness and Insomnia

Hops is often used as a mild sedative for anxiety, nervousness, and insomnia. Much of this use stems from the observation of sleepiness in European hops-pickers. *The Complete German Commission E Monographs* lists hops as an approved herb for "mood disturbances such as restlessness and anxiety, sleep disturbances."¹⁶ Although there have been no meaningful clinical studies to support hops as a sedative, several European studies have demonstrated formulas combining hops with other sedative herbs are effective for insomnia. A pilot study using a preparation containing 500 mg valerian extract combined with 120 mg hops extract at bedtime for 30 patients with mild-to-moderate, nonorganic insomnia resulted in a decline in sleep latency and wake time. Insomnia was diagnosed using a polysomnographic standard examination, and a positive treatment effect was based on two weeks of treatment with re-examination.¹⁷ Additionally, a similar hops-valerian preparation demonstrated efficacy and tolerability equivalent to benzodiaz-

epine for the treatment of nonchronic and nonpsychiatric sleep disorders.¹⁸ Combinations of hops with valerian and passionflower (*Passiflora incarnata*) or lemon balm (*Melissa officinalis*) are also approved by the German Commission E as sedative and sleep promoting formulas. Further studies are needed to determine if hops acts as a mild sedative independently, as a synergist, or is absent of sedative action.

Cancer Prevention

Three flavonoids (xanthohumol, dehydrocycloanthohumol, and isoxanthohumol) from hops caused a dose-dependent decrease in growth of human breast, colon, and ovarian cancer cells *in vitro*.⁶ Additionally, hops flavonoids induced quinone reductase (QR) in cultured mouse hepatoma Hepa 1c1c7 cells.⁹ QR is primarily a cytosolic flavoprotein that protects cells against the toxicity of xenobiotics by catalyzing the reduction of a wide variety of quinines and quinoneimines.^{19,20} Induction of QR in mouse hepatoma cells is used to assess the potential anticarcinogenic activity of components of the human diet. Additionally, topical application of humulon, one of the bitters in hops, markedly suppressed the promotion of skin tumors in mice.²¹

Drug-Botanical Interactions

Limited evidence from one animal study suggests that hops may potentiate the effects of sedative drugs.²² The phytoestrogenic effects of 8-prenylnaringenin theoretically could have an impact on hormonal therapies, although no studies have been conducted to confirm this.

Side Effects and Toxicity

Humulus lupulus is believed to be nontoxic. However, as with all plants, it may cause allergic reactions in sensitive individuals. *Humulus lupulus* is known to cause a contact dermatitis in hops-pickers, attributed to myrcene in fresh hop oil. Additionally, a mechanical dermatosis has been attributed to the rough hairs on the stem and secretions of the yellow glandular hairs on hops.²³ No clinical cases of allergy or anaphylaxis resulting from therapeutic use of hops have been published.

Dosage

A standard dosage is 500 mg one to three times daily.²⁴ Maximum safe dosages are unknown.

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