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FILE: ▪ Hops (*Humulus lupulus*)
▪ Pharmacological Profile
▪ Sedative Activity

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RE: Pharmacological Profile of Hops

Zanoli P, Zavatti M. Pharmacognostic and pharmacological profile of *Humulus lupulus* L. *J Ethnopharmacol*. 2008;116:383-396.

Hops (*Humulus lupulus*) has been used traditionally for medicinal purposes, particularly for the treatment of sleep disorders, as a mild sedative, and as a bitter for the activation of gastric function. In addition, hops was used internally and topically to relieve muscle spasms and nerve pain. Another long-time use of the plant has been in the brewing industry. Its female inflorescences (hop cones) are used to preserve beer and give it a characteristic aroma and flavor. These authors describe the morphological, phytochemical, and ethnopharmacological aspects of the plant and summarize their most interesting findings obtained in preclinical and clinical research.

According to the authors, only a few findings of *H. lupulus* exist in Europe from prehistoric periods. There are more findings from the early Middle Ages because of its increased use in the brewing process. The cultivation of hops started from the middle of the ninth century in Germany, where it extended from north to south during the early and high Medieval period, as well as to other regions of central Europe. Currently, the brewing industry accounts for 98% of the world use of hops.

Native American tribes used hops as a sedative, antirheumatic, analgesic, and as a urinary aid for "gravel" and inflammation. In India, the Ayurvedic Pharmacopoeia recommends hops to treat restlessness associated with nervous tension, headache, and indigestion. In traditional Chinese medicine, hops is used to treat insomnia, restlessness, dyspepsia, and lack of appetite.

The German Commission E and European Scientific Cooperative on Phytotherapy approved hops as a treatment for excitability, mood disturbances (restlessness, anxiety), and sleep disturbances.

The main structural classes of chemical compounds identified from mature hop cones include terpenes (0.3-1.0% dry wt.), bitter acids (5-20% dry wt.), and chalcones. They are also rich in flavonol glycosides and catechins. The bitter acids are phloroglucinol derivatives usually classified as α-acids (humulones) and β-acids (lupulones) and are present in hops as a complex mixture of variable composition and concentrations. Several prenylflavonoids have been identified from hop cones. According to the authors, the most important compound is the chalcone xanthohumol (up to 1% dry wt.), which can be converted to the prenylflavonone

isoxanthohumol (IX) with thermal treatment and increased pH value. IX can be converted by the intestinal flora and/or liver cytochrome P450 to 8-prenylnaringenin (8-PN), a potent phytoestrogen.

The authors cite a number of studies of mice and rats (including their own studies) investigating the use of different extracts of hops as a mild sedative. A CO_2 extract administered orally enhanced pentobarbital-sleep and reduced behavioral despair test immobility time, suggestive of antidepressant activity, at a 10 mg/kg dose in rats. The CO_2 extract fraction containing α-acids elicited the same effects, while the β-acid fraction appeared to provide contributory activities. "In spite of these recent studies, the identity of the active sedative principle/s of hops as well as the mechanism/s of action is still questionable," they say. No randomized, double-blind, placebo-controlled clinical trials using hops extract alone have been conducted.

Combinations of hops and valerian have shown promising results as useful and safe alternatives to the classic sedative drugs. However, say the authors, "no meaningful information regarding the potential clinical efficacy of hops can be extrapolated by using clinical formulations containing hops in combination with other medical plants. Therefore the real efficacy of hops in sleep disturbances remains to be ascertained."

The authors cite several in vivo investigations performed to study the estrogenic properties of the hop cone extracts and 8-PN. In addition, they cite a randomized, double-blind, placebo-controlled study on the use of a standardized hops extract in menopausal women, in which a decrease in hot flashes and other discomforts associated with estrogen deficiency were reported. Other studies support the plant's efficacy in relieving menopausal symptoms. "Although further clinical studies are needed, hop-derived prenylated flavonoids could provide an attractive alternative treatment for the relief of menopausal symptoms," say the authors.

During the past 10 years, several in vitro studies have been performed to evaluate the potential activity of hops components including the bitter acids as chemopreventive agents. Among the components, "xanthohumol (XH) has received the major attention because it seems to inhibit in vitro initiation, promotion, and progression stages of carcinogenesis."

The authors cite several studies reporting antibacterial and antifungal activities of certain hops constituents.

Regarding its effect on the stomach, the authors cite a study of an aqueous preparation of *H. lupulus* in patients affected by chronic hyposecretory gastritis. The study reported that the treatment stimulated gastric secretion.

Among the reported side effects of hops are bronchial irritation, dry cough, and dyspnea in hop-processing workers, as well as occupational dermatitis associated with fresh and dried hops. However, the authors note that "no clinical case of allergy or anaphylaxis resulting from the therapeutic use of hops has been published."

The authors conclude that the "use of chemically characterized hop extracts for biological assays and for clinical trials is the right approach to study their pharmacokinetic and pharmacological profile and to perform comparative studies, with the aim to validate the mentioned properties of hops." Much work is needed "to achieve a reliable standardized product and to link it to a specific biological activity and to specific therapeutic applications."

—Shari Henson

The American Botanical Council has chosen not to include the original article.