REFERENCES

HOPS
Humulus lupulus

Schauenberg, P., **Paris**, F.: Guide to Medicinal Plants. 1990 First paperback edition (Paris 1974). Lutterworth Press ISBN No. 0-7188-2820-8.

Schauenberg and Paris say that it is widespread in its occurrence. The cones of the hop contain lupoline, a complex substance formed from various ketones: humulone, lupulone, resins, luparol, choline and asparagine. It is antibiotic, oestrogenic, hypnotic, sedative. As the plant cannot be preserved for any length of time, these qualities are of little value. Used in beer as an aromatic bitter and as a bacteriostatic agent. It is used as a hypnotic and a mild sedative in some herbal recipes which employ the concentrated extract. In homoeopathy a tincture of the fresh cones is used as a narcotic, a diuretic and an aphrodisiac. The use of hops in the brewery trade dates from the Middle Ages. Its medicinal value was discovered at the start of the 19th. century.

Newall, Carol A.; **Anderson**, Linda A. and **Phillipson**, J. David: Herbal Medicines - a guide for health-care professionals. London. The Pharmaceutical Press. 1996. ISBN No. 0-85369-289-0.

HOPS

Species (Family)
Humulus lupulus L. (Cannabinaceae/Moraceae)

Synonyms(s)
Humulus, Lupulus

Part(s) Used
Strobile.

Pharmacopoeial Monographs
BHP 1983
BHP 1990
BPC 1949
Martindale 28th edition

Legal Category (Licensed Products)
GSL

Constituents
Flavonoids Astragalin, kaempferol, quercetin, quercitrin, rutin
Chalcones Izoxanthohumol, xanthohumol, 6-isopentenyl-naringenin, 3'-(isoprenyl)-2',4-dihydroxy-4',6'-dimethoxychalcone, 2',6'-dimethoxy-4,4'-dihydroxychalcone.
Oleo-resin(3 - 12%). Various phenolic compounds including α-bitter acids (e.g. humulone, cohumulone, adhumulone, prehumulone, posthumulone), β-bitter acids (e.g. lupulone, colupulone, adlupulone), and their oxidative degradation products including 2-methyl-3-buten-2-ol.

Tannins (2 - 4 %) Condensed; gallocatechin identified.
Volatile oils (0.3 - 1.0%) More than 100 terpenoid components identified; primarily (at least 90%) β-caryophyllene, farnescene, and jumulene (sesquiterpenes), and myrcene (monoterpene).
Other constituents Amino acids, phenolic acids, gamma-linoleic acids, lipids, oestrogenic substances (disputed).

Food Use
Hops are listed by the Council of Europe as a natural source of food flavouring (category N2). This category indicates that hops can be added to foodstuffs in small quantities, with a possible limitation of any active principle, (as yet unspecified) in the final product.

Herbal Use
Hops are stated to possess sedative, hypnotic, and topical bactericidal properties. Traditionally they have been used for neuralgia, insomnia, excitability, priapism, mucous colitis, topically for crural ulcers, and specifically for restlessness associated with nervous tension headache and/or indigestion.

Dose
Dried strobile 0.5 - 1.0 g or by infusion; 1 - 2 g as a hypnotic
Liquid extract (1:1 in 45% alcohol) 0.5 - 2.0 ml
Tincture (1:5 in 60% alcohol) 1 - 2 ml.

Pharmacological Actions
Animal studies Anti-bacterial activity, mainly towards Gram-positive bacteria, has been documented for hops and attributed to the humulone and lupulone constituents. The activity of the bitter acids towards Gram-positive bacteria is thought to involve primary membrane leakage. Resistance of Gram-negative bacteria to the resin acids is attributed to the presence of a phospholipid-containing outer membrane, as lupulone and humulone are inactivated by serum phospholipids. Structure activity studies have indicated the requirement of hydrophobic molecule and a six-membered central ring for such activity.

The humulones and lupulones are thought to possess little activity towards fungi or yeasts. However, antifungal activity has been documented for the bitter acids towards *Trichophyton, Candida, Fusarium* and *Mucor* species, and anti-bacterial activity towards *Staphylococcus aureus*.

Anti-spasmodic activity has been documented for an alcoholic hop extract on various isolated smooth muscle preparations. Hops have been reported to exhibit hypnotic and sedative properties. 2-Methyl-3-buten-2-ol, a bitter acid degradation product, has been identified as a sedative principle in hops. 2-Methyl-3-buten-2-ol has been shown to possess narcotic properties in mice and motility depressant activity in rats, with the latter not attributable to a muscle-relaxant effect. It has also been suggested that isovaleric acid residues present in hops may contribute towards the sedative action.

Hops have previously been reported to possess oestrogenic constituents. However, when a number of purified components, including the volatile oil, and the bitter acids, were examined using the uterine weight assay in immature female mice, no oestrogenic activity was found.

Human studies The documented human studies generally refer to hops given in combination with one or more additional herbs. Hops have been reported to improve sleep disturbances when given in combination with valerian. It has been stated that only low amounts of 2-methyl-3-buten-2-ol, the sedative principle identified in hops, are present in sedative tablets containing hops. However, it is thought that 2-methyl-3-buten-2-ol is formed *in vivo* by metabolism of the α-bitter acids, and therefore, the low amount of 2-methyl-3-buten-2-ol in a preparation may not indicate low sedative activity. Interestingly, relatively high concentrations of 2-methyl-3-buten-2-ol were found in bath preparations, suggesting that high concentrations of 2-methyl-3-buten-2-ol may be achieved in both tea and bath products containing hops.

Hops, in combination with chicory and peppermint, have also been documented to relieve pain in patients with chronic cholecystitis (calculous and non-calculous). A herbal product containing a mixture of plant extracts, including hops and uva-ursi, and alpha tocopherol acetate has improved irritable bladder and urinary incontinence. Excellent results were reported for 772 out of 915 patients.

Side-effects, Toxicity
Respiratory allergy caused by the handling of hop cones have been documented; a subsequent patch test used dried, crushed flower heads proved negative. Positive patch test reactions have been documented for fresh hop oil, humulone, and lupulone. Myrcene, present in the fresh oil but readily oxidised, was concluded to be the sensitising agent in the hop oil. Contact dermatitis to hops has long been recognised and is attributed to the pollen. Small doses of hops are stated to be non-toxic. Large doses administered to animals by injection have resulted in a soporific effect followed by death, with chronic administration resulting in weight loss before death.

Contra-indications, Warnings
It has been stated that hops should not be taken by individuals suffering from depressive illness, as the sedative effect may accentuate symptoms. The sedative action may potentiate the effects of existing sedative therapy and alcohol. Allergic reactions have been reported for hops, although only following external contact with the herb and oil.

Pregnancy and lactation *In vitro* anti-spasmodic activity on the uterus has been documented. In view of this and the lack of toxicity data, the excessive use of hops during pregnancy and lactation should be avoided.

Pharmaceutical Comment
The chemistry of hops is well documented and is characterised by the bitter acid components of the oleo-resin. Documented pharmacological activities justify the herbal uses, although excessive use should be avoided in view of the limited toxicity data.

Alexander, P: Nature's Store. Manufacturing Chemist October 1990, p33-40.

In an article we read that a phytohormone complex is said to help prevent premature skin aging.

Probert Jones, Christina: Marks and Spencer: Extracts from Nature. 1989 Tigerprint. no

ISBN No.

In the Extracts from Nature Book we learn that it was used by the ancients as a tonic, hops were introduced to England by the Dutch in the 16th century. As a sedative it is used to treat irritability, tension, restlessness and indigestion. It also acts as an anaphrodisiac in men and is antiseptic and diuretic.

Back, P.. The Illustrated Herbal. 1987. Hamlyn Publishers through Octopus Books printed in Hong Kong by Mandarin. ISBN No.0 600 553 361.

In a reference from Back we read that hops were not allowed to be cultivated on a large scale in Britain until the 17th century. The hop is a tonic herb and helps to improve the appetite and digestion. Hops are good for curing sleeplessness without causing a headache.

An infusion of hops is good for toning up the system. An infusion made using equal parts of hops and chamomile can be used to help relieve painful swellings and boils. For earache, a small bag stuffed with warmed fresh hops is said to bring relief. Hop-filled pillows are well known to help those who suffer from sleeplessness.

Mills, S.Y.: The A-Z of Modern Herbalism, A comprehensive guide to Practical Herbal Therapy. Thorsons 1989 (retitled) ISBN No. 0-7225-1882-X. signed edition.

Mills says that it is found through Europe to Asia and southern England in hedgerows, thickets and open woods. It contains volatile oil and bitter resin complex (together referred to as lupulin), condensed tannins, oestrogenic substances, asparagin.

It is sedative, visceral antispasmodic, bitter digestive tonic, locally antiseptic and healing.

Applications: to visceral smooth muscle tensions affecting digestive and bowel function (e.g. nervous dyspepsia and colitis, spastic constipation); as a bitter tonic to digestion; as a sedative to encourage restfulness and sleep and reducing symptoms of nervous tension; as an inhalant to induce sleep. CAUTION:- avoid in depressive illness.

Powell, E.F.W.: The Natural Home Physician, A Book for Every Household. Health Science Press 1981 reprinted 2nd ed. ISBN No. 0-85032-092-5.

Powell says that it is a fine old remedy for nervousness and insomnia. An old country custom was to stuff a pillow with Hops and sleep with the head resting on the pillow. Evidence is to hand to show that this helped to cure some bad cases of sleeplessness. Hop pillows may cause drowsiness during the day, especially when the individual is sensitive to the remedy.

Howard, M.: Traditional Folk Remedies, A comprehensive Herbal. Century paperbacks. 1987. ISBN No. 0-7126-1731-0.

Howard says that it is also known as Hop bine, willow wolf. The common name is said to originate in Old English hopen or hoppan, meaning 'to climb'. Its most known use is in beer brewing. The oil from the hops is used in perfumery, it is also a popular ingredient for herb pillows and was used in the Middle Ages as a cure for insomnia. Hop tea, widely used in folk medicine as a general tonic, was said to aid the digestion. A brown dye can be distilled from the

leaves and flowers.

It is sedative, tonic, diuretic, nervine and antibiotic. Hops are generally recommended for treating insomnia and nervous disorders because they are a sedative. They also have limited effect in cases of water retention.

Hooper, M.: Herbs and medicinal plants 1984, 1989 Kingfisher Books ISBN No. 0-86272-484-8.

Hooper says that a tea made from hops and a teaspoon of honey is a good tonic and sedative. The hop can also be blended with Indian teas. Small muslin bags stuffed with dried hops can be slipped into pillow cases to help sufferers of insomnia, and in the past the khaki dyes needed for army uniforms were also made from hops.

The Lawrence Review of Natural Products. Copyright 1994 by Facts and Comparisons (ISSN 0734-4961). 111 West Port Plaza Suite 400, St. Louis, Missouri 63146-3098.

In the Lawrence review of natural products we read that hops are known by the scientific Names: *Humulus lupulus* L. Family: Moraceae or Cannabaceae.

Common Names: Hops, European hops, common hops, lupulin

BOTANY - Hops are climbing perennial plants with male and female flowers on separate plants. Hops can attain heights of 25 feet. The plan is cultivated throughout the world. Commercially, the female cone-like flowering parts are collected and dried. Lupulin is composed of the separated glandular hairs, and contains more resins and volatile oil than hops, although it may also contain more adulterants.

HISTORY - The major use of hops is in the production of beer, where oxidation of the bitter principle humulene yields the characteristic flavour. Extracts are used as flavours in the food and beverage industry.

Traditionally, hops had been used as a diuretic and in the treatment of intestinal cramping, tuberculosis, cancer and cystitis. Brewery sludge baths had been used medicinally for their rejuvenating effects and for the treatment of menstrual problems.

As sedation was sometimes observed in hop pickers, the flowers were used as sedatives and were sometimes placed in pillows to relieve nervous conditions. Some extracts are used as emollients in skin preparations.

CHEMISTRY - A complex mixture of compounds has been identified in hops and volatile oil, with more than 100 compounds having been characterized. The oil comprises approximately 1% of the plant. Resinous bitter principles are found in the plant and related compounds, lupulone and related compounds, and other resins.

The volatile oil comprises primarily humulene (alpha-caryophyllene), myrcene, beta-caryophyllene and farnesene, which account for more than 90% of the oil fraction. The gas chromatographic analysis of the essential oil often permits the identification of hops varieties, an often difficult task to accomplish using standard botanical characteristics.

PHARMACOLOGY - A number of pharmacologic activities have been ascribed to hops extracts. The bitter acids (lupulone, humulone, etc)(are reported to have antimicrobial activity, with the more hydrophobic compounds being the most active.

In addition the extract are said to inhibit smooth muscle spasticity. A volatile alcohol, 2-methyl-3-butene-2-ol may account in part for the sedative and hypnotic effects of the plant.

A number of reports have suggested that hops contain compounds that impart oestrogenic activity. An early study by Zenisek and Bednar found a high level of oestrogenic activity in the beta-bitter acid fraction of the plant. One poorly designed study (which subsequently became something of a legend) reported that women who participated in hops collection often began menstruating 2 days after starting to reap the hops. However, neither oestrogenic nor any other hormonal activity has been observed in a variety of hops extracts tested in several animal models under carefully controlled conditions.

Hops are closely related botanically to marijuana, and the smoking of hops as a mild sedative has been described.

TOXICOLOGY - Extracts can be allergenic with contact dermatitis having been reported after exposure to hops pollen. However, bronchial hyperresponsiveness among hops packagers occurred with an incidence similar to that observed in the normal population.

SUMMARY - Hops are used widely in the commercial preparation of beer, where the degradation of certain components yields the characteristic flavour.

Hops extracts have been used for a variety of medicinal purposed throughout the ages, although most of these uses have not persisted. Although hops had been used in the management o numerous "female disorders", is not evidence that hops possess oestrogenic or other hormonal activity.

Keville, K.: The Illustrated Herb Encyclopaedia - a complete culinary, cosmetic, medicinal and ornamental guide to herbs. Grange Books. 1991. ISBN No. 1-85627-175-7.

Keville says that *Humulus lupulus* was previously known as *Humulus americanus* and is native to Europe. Hops are found in the wild in thickets with damp, dep humus-rich soils. Cultivated in Europe and Chile.

It contains lupulin; essential oil (0.3-1%) includes hupulene; bitter resin (3-12%); also flavonoids (astralagin, quercitrin, rutin); estrogenic substances, asparagin; GLA.

The Roman historian Pliny dubbed hops lupus, or wolf, after noticing the way it twines tightly around other plants, The word hops comes from hoppan, "to climb". Hops were grown by the Romans but were not widely cultivated until the 9th and 10th centuries, mainly in France and Germany. In less than 100 years a new drink called bier made from Bavarian hops became famous. It was developed after hops was added to bread to encourage fermentation and preservation. Since bread was sometimes used in brewing, it was discovered that hops increased the beer's alcohol content. The English, however, continued to make the traditional ales, flavoured with bitters like alehoof and alecost (costmary and ground ivy) and preferred to sleep

on hops pillows instead. In the 15th century, Henry VIII warned that humele was a wicked weed that "would spoil the taste of the drink and endanger the people" and forbade its use. In the 17th century the English herbalist John Evelyn was still claiming that ingesting hops could result in disease, melancholy and a shorter life. In Russia, the word hmel describes both the herb and a slightly drunk person.

Medicinally. The strobiles of hops are mildly sedative and diuretic. They are a bitter digestive that is especially suited for treating nervous indigestion, ulcers, insomnia, irritable bowel syndrome, and Crohn's disease. They relax nerves and smoothe muscles, especially in the digestive tract, within 20-40 minutes after ingestion. A 1980 study suggested that they contain a muscle relaxant constituent in addition to lupulin, which had been assumed to be the only active chemical. Hops' antibacterial agents, responsible for preserving bread and beer, also fight digestive tract infections. Hormonal effects from estrogen-like compounds were first noted when female hop pickers experienced changes in their menstrual cycles (some even stopped menstruating) aftyer absorbing quantities of the essential oil through their hands. Aphrodisiacal effects were observed in men. Regular doses of the herb can help regulate the menstrual cycle. GLA (gamma linolenic acid), which occurs in the evening primrose oil, has been found in hops, suggesting its usefulness for PMS and menstrual problems, especially muscle cramps, headaches and sore breasts. Hops also helps insomniacs. A hop poultice can relieve the pain and inflammation or earache or toothache. Experiments in Germany have shown that hops tincture are more stable than dried hops which quickly degrade with exposure to light and humidity.

Aromatherapy. A hops "sleep pillow" encourages a sound sleep. Europeans used to fill a whole bed pillow with the strobiles, but a small hops pillow tucked under the usual bed pillow is all that is needed. Apparently the fragrance is responsible for the soporofic action.

In cosmetics it is used in skin softening creams and lotions, its effectiveness is possibly due to hormonal actions.

Up to 30% of hop pickers experience some degree or dermatitis, with pollen from the strobiles causing skin eruptions in about 1 out of every 300.

Bianchini F., **Corbetta** F,.: The Fruits of the Earth. Translated from the Italian by Mancinelli A.Bloomsbury Books, London. ISBN No. 1-870630-10-6.

Bianchini says that *Humulus lupulus* is a very common plant, found wild or cultivated, in Europe, Asia and North America. Its commercial ijmportance is in themaking of beer for which the cones of the female plant are used. The hop has estrogenic action, feminising and aphrodisiac, so that, besides serving as a sedative, it is believed by some to be the cause of disorders (obesity, sterility, hepatic degeneration) afflicting hard beer drinkers. The hop shoots, that is, the edible shoots of the panicle, are eaten on the Continent as a vegetable. They are boiled in salt water with a little lemon.

Hutchens, A.R.: Indian Herbalogy of North America. 1973 First paperback edition. Shambhala. ISBN No. 0-87773-639-1.

Hutchens says that the hop plant is one of the few crop plants in which male and female flowers are borne on different plants. Introduced and cultivated in the U.S. for its cones and strobiles, which are used medicinally and in the manufacture of beer, ale and porter.

Lupulin is preferred to the hops itself and is procured by beating or rubbing the strobiles and then sifting out the grains, which form about one seventh of the hops. Lupulin is a globose, kidney-shaped grain, golden yellow and somewhat transparent. This substance is the bitter principle of hops, and is used in aqueous solutions of Lupulin.

The strobiles or cones are used medicinally for their tonic, diuretic, nervine, anodyne, hypnotic, anthelmintic, sedative, febrifuge effect.

The decoction of hops cleanses the blood, making it useful in venereal diseases and all kinds of skin abnormalities such as itch, ringworm, spreading sores, tetters and discolorations. It will tone up the liver, assist a sluggish gall bladder, and will increase the flow of urine. Principally used for sedative or hypnotic action, producing sleep, removing restlessness and allleviating pain, especially so if combined with chamomile flowers. Used both internally and externally.

The lupulin tincture is used in delirium tremens, nervous exhaustion, anxiety, worms, and does not disorder the stomach or cause constipation. Also useful in after-pains and to mitigate the pain attending gonorrhoea.

A pillow made of the dried hops, sprinkled with alcohol to bring out the active principle, is used for wakefulness and generally induces sleep.

Externally: An ointment made by boiling 2 parts of *Stramonium* (Jimson Weed) and 1 part hops, in lard, is an excellent application in skin irritation and itching skin.

Russian experience: Hmel is the Russian name for hops, which to them (and us) is an expression for persons that are slightly drunk.

Folk Medicine: The medical properties have long been appreciated for success as diuretic, sedative and calming. Used for inflammation of the bladder, tuberculosis and as hair tonic. The root decoction for jaundice and dandruff.

Weiss, R.F.. Herbal Medicine. (translated from the 6th. German edition of Lehrbuch der Phytotherapie by A.R.Meuss). The Bath Press. 1986. ISBN 0-906584-19-1.

Weiss says that the hop plant, *Humulus lupulus*, is a climbing plant often found in alder-swamps and damp hedges. The drug comes from cultivated plants, and hops are a major crop in some parts, mainly for use in beer brewing. On the other hand, hops are also a valuable drug. The glossy yellow glands on the cone-like fruits (strobiles) contain between 1% and 3% of a volatile oil and considerable quantities of a resin with two bitter principles lupamaric acid (humulone) and lupulinic acid. On storage these convert to isovaleric acid. The action is one of central depression, as with fresh hops, and varies depending on the variety of hops. The term used for the drug and preparations made from it are not always correctly used, resulting in serious misunderstandings.

Strobili Lupuli (dried strobiles). The strobiles consist of numerous individual fruits (achenes), each behind its own leaf like bract. These bracts overlap like roof tiles, giving the strobiles their characteristic appearance. The bracts and the axis of the strobile are studded with many small yellow glands. These are the active component of the drug, yielding the medicinal principle.

Glandulae Lupuli (lupulin). These are the small yellow glands removed from the freshly dried strobiles by sieving. It should be noted that lupulin is not the pure principle, merely the glands separated from the strobile. It is a fine powder.

Hops are a mild sedative, probably not quite as effective as valerian. On the other hand this drug has some special features. It is considered to be particularly helpful with sleep problems, and it is also said to be particularly effective against sexual excitement. Added to this is a stimulant effect on the stomach due to the bitter principles. This points to three areas where hops can be particularly useful; sleeplessness, nervous gastropathies, and sexual neuroses (wet dreams, premature ejaculation, and as an anaphrodisiac in general for men).

Some typical recipes are given.

A tisane made with fresh hops is a folk remedy for sleeplessness. Alternatively, a small pillow would be filled with hops and placed under the head at night to encourage sleep.

It was girls and women picking hops who first drew attention to the fact that hops have an effect on genital organs. Before machines were introduced, hop pipckers used to spend several weeks at this work, and it had always been known that menstrual periods would come early in young girls while they were there. Today we know the reason. Hops contain plant hormones, particularly when very fresh, and these are similar to oestrogens. Considerable amounts have been found, 30,000 to 300,000 i.u. of oestrogen in 100g of hops. This also explains why hops will suppress sexual excitement in men. It has been shown that there are substances called anti-androgens that are able to cancel the effects of the male hormone (androgen).

It is possible that hops contain a similar principle in the form of a plnt hormone. This has not yet been identified, but it could provide an explanation for the actions of the drug.

British Herbal Pharmacopoeia, The: 1983. ISBN 0-903032-07-4. British Herbal Manufacturers Association (B.H.M.A):

HUMULUS
Hops, Lupulus

Humulus consists of the dried strobiles of *Humulus lupulus* L. (Family: Cannabinaceae) collected from the female plant. It is natibve to Britain.

Humulus contains volatile oil consisting chiefly of humulene, bitter principles and tannins.

Martindale 25th edition, p.618. BPC (1923), p.637. BPC (1934), p.610-611. BPC (1949), p.1456. BP (1889), p.208.

Therapeutics
Action: Sedative, hypnotic. Topically bactericidal.
Indications: Neuralgia. Insomnia. Excitability. Priapism. Mucous colitis.
Topically: Crural ulcers.
Specific Indications: Restlessness associated with nervous tension headache and/or indigestion.
Combinations used: Combines well with Valeriana as hypnotic and with Chamaemelum for

nervous dyspepsia.
Contra-indications: Inadvisable in depression.
Preparations and dosage: Dose 0.5-1 g: as hypnotic; 1-2 g; or by infusion. Liquid Extract 1:1 in 45% alcohol. Dose 0.5-2 ml. Tincture 1:5 in 60% alcohol 1-2 ml.

Council of Europe. Plant Preparations used as ingredients of cosmetic products. 1st. edition. Strasbourg 1989. HMSO. ISBN No. 92-871-1689-X

Humulus lupulus L
Family: Cannabinaceae

Common names: Hop (English CTFA name), Houblon (French), Hopfen (German), Luppolo (Italian), Lupulo (Spanish), Hop (Dutch).

The cones (flowers) are used.

Chemical composition

- Essential oil 0.2-0.8%
(- Myrcene 30-50%, α- and ß-caryophyllene 50%, farnesene, dipentene, p-cymene, linalool, geraniol, myrcenol and esters.
  - Formic, acetic, butiric (butyric?), valerianic, caprilic (caprylic?), capric, enanthic, pelargonic acid and esters.
  - Sesquiterpene: 2,6-dimethyl-10-methylene-2,6,11-dodecatriene
  - Methylnonylketone
- Resins (humulon, adumulon, coumulon, humulinon (α fraction) and lupulon, colupulon, adlupulon (ß fraction).
- Flavonoids 0.2-0.8% (quercetin, astragalin, kaempferol, rutin, isoquercetrin)
- Leucoanthocyanidins (leucocyanidin, leucodelphinidin)
- Proteins, amino acids, amides, amines
- Phytosterols
- Phytoestrogens
- Glucides
- Tannins

Intended cosmetic effects and recommended maximum concentration in cosmetic products

Tonic, astringent, firming, emollient, lenitive

1-2% glycolic extract and oil tincture in relaxing baths, products for supposed firming and anti-wrinkle effect.

Other possible effects

Sedative, antiseptic, flavouring

Toxicological data

(humulon) o anim.

Evaluation and remarks

Group 2

Selected toxicological references

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Fenselau P. and Talalay A. (1973). Is oestrogenic activity present in hop? Food Cosmet. Toxicol. 11, 597-603.

Y. **Okano**, K. **Rin**, N. **Okamoto**, T. **Yamamura** and H. **Masaki**: Hop extract as a new potent ingredient for hair growth. Preprint - Platform Presentation Vol.3. 18th International I.F.S.C.C. Congress. Venice, Italy 3.10.1994.

Summary

80 plant materials were examined on hair growth. First, in vitro screening tests were examined to select the active ingredients in hair growth. The inhibition of 5α-reductase was used in vitro as a chemical evaluation. From the biological aspect we evaluated the hair follicle derived keratinocyte (HFK) proliferation suppressed by androgen and the growth activity of HFKs.

It was found that hop (*Humulus lupulus* L.) strongly inhibited the activity of 5α-reductase and recovered the proliferation of HFKs suppresses by TE and DHT. Under the test conditions deoxycorticosterone acetate (DOCA), a typical inhibitor of 5α-reductase, showed a weak effect on the recovery.. The recovery effect of the hop extract was strongly expressed when suppressing DHT. We compared the stimulatory effect of the hop extract on HFK proliferation with minoxidil (MX), a typical active agent in hair growth products. Hop extract raised the proliferation to 28% at 6.25 μg/ml in contrast to 10% at 1.25 μg/ml for MX. It was found that hop extract not only recovered the proliferation of HFKs suppressed by androgen but also stimulated the proliferation of HFKs. Furthermore, the effects of hop were evaluated using both animal tests and human volunteers in vivo. It was demonstrated that hop showed a potent acceleration on hair growth.

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Wohlfart R **Wurm** G **Hansel** R **Schmidt** H: [Detection of sedative-hypnotic active ingredients in hops. 5. Degradation of bitter acids to 2-methyl-3-buten-2-ol, a hop constituent with sedative-hypnotic activity]. Nachweis sedativ-hypnotischer Wirkstoffe im Hopfen, 5. Mitt. Der Abbau der Bittersauren zum 2-Methyl-3-buten-2-ol, einem Hopfeninhaltsstoff mit sedativ-hypnotischer Wirkung. Arch Pharm (Weinheim) (1983) 316(2):132-7 (Published in German). [No Abstract Available]

Hansel R **Wagener** HH: [Attempts to identify sedative-hypnotic active substances in hops]. Versuche, sedativ-hypnotische Wirkstoffe im Hopfen nachzuweisen. Arzneimittelforschung (1967 Jan) 17(1):79-81 (Published in German). [No Abstract Available]

Mannering GJ **Shoeman** JA **Shoeman** DW: Effects of colupulone, a component of hops and brewers yeast, and chromium on glucose tolerance and hepatic cytochrome P450 in nondiabetic and spontaneously diabetic mice. Biochem Biophys Res Commun (1994 May 16) 200(3):1455-62.

Brewers yeast contains factors that increase and decrease glucose tolerance. Hop components (lupulones) that adhere to yeast during the brewing process elicit a variety of biological effects including the induction of hepatic cytochrome P4503A. Colupulone was tested for its effects on glucose tolerance and cytochrome P450. Serum glucose levels 30 min after the injection of glucose were lowered by colupulone in nondiabetic Swiss-Webster mice, elevated in diabetic C57B1/KSJ-db/db mice, and unaffected in nondiabetic C57B1/KSJ+m/+m mice. Colupulone lowered hemoglobin glycation slightly in +m/+m mice but not in db/db mice. The cytochrome P450 system was highly induced by colupulone in both db/db and +m/+m mice. Chromium, which acts in concert with the factor in yeast that enhances glucose tolerance, had little or no effect on the plasma glucose level or the cytochrome P450 system in either +m/+m or db/db mice.

Bravo L **Cabo** J **Fraile** A **Jimenez** J **Villar** A: [Pharmacodynamic study of the lupulus' (Humulus lupulus L.) tranquilizing action]. Estudio farmacodinamico del lupulo (Humulus lupulus L.). accion tranquilizante. Boll Chim Farm (1974 May) 113(5):310-5 (Published in Spanish). [No Abstract Available]

Mannering GJ **Shoeman** JA **Deloria** LB: Identification of the antibiotic hops component, colupulone, as an inducer of hepatic cytochrome P-4503A in the mouse. Drug Metab Dispos (1992 Mar-Apr) 20(2):142-7.

A higher level of cytochrome P-450 (P450)-dependent ethylmorphine (EM) N-demethylase activity was observed in hepatic microsomes from mice fed a natural-ingredient diet ("crude diet") than in those from mice fed a semi-purified diet ("purified diet"). This led to the testing of individual ingredients of the crude diet as inducers of the P-450 system. Brewers yeast proved to be the most significant inductive component of the crude diet. Further investigation revealed that hop components (lupulones) absorbed on yeast during the brewing process were responsible for the induction of the P-450 system. The induction of P-450 and several P-450-dependent monooxygenase activities (EM N-demethylation, aniline hydroxylation, benzo[a]pyrene hydroxylation) by colupulone with respect to dose and time course were investigated. The very large increase in EM N-demethylase activity elicited by colupulone suggested that P-4503A had

been induced. Western blot technology verified this speculation. Western blot analysis of microsomal protein from mice fed hops, brewers yeast, or the residue of a hexane extract of hops supported the conclusion that all of these substances induced P-4503A. These substances were also relatively good inducers of P-4502B, but not as inductive of this isozyme as the crude diet. This is interpreted to mean that not all of the inductive properties of the crude diet are due to hop components. These studies question the use of crude commercial diets in studies of P-450 systems. They may also challenge some current definitions of "constitutive" and "induced" P-450s.

Williams CS **Eastoe** BV **Slaiding** IR **Walker** MD: Analysis of pesticide residues in hops and their extraction by liquid CO2 during the production of hop extracts. Food Addit Contam (1994 Sep-Oct) 11(5):615-9.

A method has been developed for analysing pesticide residues in whole hops, hop pellets and hop extracts by GC-MS. Five batches of hop pellets containing nine different pesticides (triadimefon, dicofol, mephosfolan, bupirimate, cyhalothrin, tetradifon, endosulfan, pyrazophos and total bisdithiocarbamates) were extracted with liquid CO2. Pesticide concentrations in the original hop pellets and the extracts were determined. The pesticides were concentrated by the extraction process (concentration factor 1.3-8.3), except for the bisdithiocarbamates, which were not extracted. When the same amount of bitterness was added into the brewing process using liquid CO2 extract as opposed to hop pellets, for most of the pesticides proportionately less pesticide was added. However, for two pesticides (dicofol and triadimefon) corrected residue levels were similar to, or in some cases slightly higher than, those in hop pellets.

Shipp EB **Mehigh** CS **Helferich** WG: The effect of colupulone (a HOPS beta-acid) on hepatic cytochrome P-450 enzymatic activity in the rat. Food Chem Toxicol (1994 Nov) 32(11):1007-14.

Colupulone, a component of hops, was examined for its ability to alter rat hepatic cytochrome P-450 enzymatic activity, expression of hepatic cytochrome P-450 mRNA, and in vitro promutagen activation. Colupulone was fed to male Sprague-Dawley rats for 5 days at 0.36% in the modified AIN 76 diet. Three cytochrome P-450 enzymatic activities were measured, and the corresponding steady-state mRNA levels were examined by Northern blot hybridization. Colupulone increased cytochrome P450IIB and P450IIIA steady-state mRNA levels. In vitro promutagen activation was measured in the Ames assay using liver homogenates from each treatment group. Colupulone treatment did not alter the ex vivo cytochrome P-450-mediated activation of aflatoxin B1 or benzo[a]pyrene to their mutagenic forms. The effect of long-term colupulone administration on in vivo cytochrome P-450 enzymatic activity remains to be determined.

Fenselau C **Kelly** S **Salmon** M **Billets** S: The absence of tetrahydrocannabinol from hops. Food Cosmet Toxicol (1976 Jan) 14(1):35-9. [No Abstract Available]

Fenselau C **Talalay** P: Is oestrogenic activity present in hops? Food Cosmet Toxicol (1973 Aug) 11(4):597-603. [No Abstract Available]

Nitz S **Moza** P **Korte** F: A capillary gas-liquid chromatographic method for determination of ethylenethiourea and prophylenethiourea in hops, beer, and grapes. J Agric Food Chem (1982 May-Jun) 30(3):593-6. [No Abstract Available]

Wallen SE **Marshall** HF Jr: Protein quality evaluation of spent hops. J Agric Food Chem (1979 May-Jun) 27(3):635-6. [No Abstract Available]

Verschuere M **Sandra** P **David** F: Fractionation by SFE and microcolumn analysis of the essential oil and the bitter principles of hops. J Chromatogr Sci (1992 Oct) 30(10):388-91. Supercritical fluid extraction (SFE) is evaluated and optimized for the enrichment and fractionation of the essential oil and the bitter principles of hops (Humulus lupulus), both of which contribute to the flavor of beer. Profiles of the essential oil of different hop varieties are compared. The bitter principles, the humulones and lupulones, are analyzed by miniaturized liquid chromatography (micro-LC) and by micellar electrokinetic chromatography (MEKC).

Haas LF: Neurological stamp. Humulus lupulus (hop). J Neurol Neurosurg Psychiatry (1995 Feb) 58(2):152. [No Abstract Available]

Langezaal CR **Chandra** A **Scheffer** JJ: Antimicrobial screening of essential oils and extracts of some Humulus lupulus L. cultivars. Pharm Weekbl Sci (1992 Dec 11) 14(6):353-6.

The essential oils as well as solvent extracts of 11 hop cultivars, 1 hop variety and a wild type of hop were screened for their antimicrobial activities using the agar overlay technique. The oils were isolated from the cones of the various hop plants by hydrodistillation, the extracts were obtained by soaking the hop cones in chloroform. The oils and the extracts showed activity against the Gram-positive bacteria (Bacillus subtilis and Staphylococcus aureus) and the fungus (Trichophyton mentagrophytes var. interdigitale), but almost no activity against the Gram-negative bacterium (Escherichia coli) and the yeast (Candida albicans) used in the screening. The peak area percentages of the main volatile components and the contents of the bitter acids of the extracts were determined for all cultivars using chromatographic methods.

Wohlfart R **Hansel** R **Schmidt** H: [The sedative-hypnotic action of hops. 4. Pharmacology of the hop substance 2-methyl-3-buten-2-ol]. Nachweis sedativ-hypnotischer Wirkstoffe im Hopfen. 4. Mitteilung: Die Pharmakologie des Hopfeninhaltsstoffes 2-Methyl-3-buten-2-ol. Planta Med (1983 Jun) 48(2):120-3. (Published in German). [No Abstract Available]

Meznar B **Kajba** S: [Bronchial responsiveness in hops processing workers]. Bronhijalni odgovor u hmeljarskih radnika. Plucne Bolesti (1990 Jan-Jun) 42(1-2):27-9. (Published in Serbo-Croatian, Roman).

In small group of workers (n = 17) who had been during their working process (storing and packing of hop) exposed to the inhalation of hop dust, the bronchial responsiveness with metacholine was studied according to cumulative method. Although 70% of examined subjects had clinically pronounced signs of bronchial irritation and 50% of them the signs of chronic bronchitis, the moderately increased bronchial responsiveness was found in only 12.5% of examined subjects (n = 2) which is--due to the data from the literature--the normal percent for healthy population.

Kammerer E: [Phytogenic sedatives-hypnotics--does a combination of valerian and hops have a value in the modern drug repertoire?]. Pflanzliche Sedativa-Hypnotika--Hat eine Kombination von Baldrian und Hopfen ihre Berechtigung im modernen Arzneimittelrepertoire? Z Arztl Fortbild (Jena) (1993 Apr 12) 87(5):401-6. (Published in German). [No Abstract Available]

Tressl R **Friese** L: [Determination of aroma substances in Spalter hops by gaschromatography-mass spectrometry (author's transl)]. Gaschromatographisch-massenspektrometrische Untersuchung der Aromastoffe von Spalter Hopfen. Z Lebensm Unters Forsch (1978 Jul 31) 166(6):350-4. (Published in German).

The volatiles of Spalter hops were concentrated by destillation-extraction, separated by liquid solid chromatography and characterized by capillary gas chromatography-mass spectrometry. 125 constituents (terpenes, sesquiterpenes, esters, alcohols, acids) were identified and semiquantified.

Hansel R **Wohlfart** R **Coper** H: [Sedative-hypnotic compounds in the exhalation of hops, II]. Versuche, sedativ-hypnotische Wirkstoffe im Hopfen nachzuweisen, II. Z Naturforsch [C] (1980 Nov-Dec) 35(11-12):1096-7. (Published in German)

Hops are told to promote sleep; manyfold efforts to detect the soporific principle have been unsuccessful so far. Preliminary pharmacological tests lead to the conclusion that the soporific activity of the exhalation of hops can be explained by its content of 2-methyl-3-butene-2-ol (1) in the volatile fraction. It was found that 1, when given to mice i.p. (0.80 g/kg) produces narcosis for about 8 h; no abnormal behaviour was observed there upon. Due to its water-solubility the concentration of 1 in the essential oil obtained by steam-distillation is low; contrary to that, 1, is enriched in the more volatile fraction of hops.

FURTHER SEARCHES OF MEDLINE, MAY BE DUPLICATES

Newmark FM; Hops allergy and terpene sensitivity: an occupational disease. Ann Allergy (1978 Nov) 41(5):311-2. ISSN: 0003-4738. [No Abstract Available]

Caujolle F Pham-Huu-Chanh Duch-Kan P Bravo-Diaz L: [Spasmolytic action of hop (Humulus lupulus, Cannabinacees)] Etude de l'action spasmolytique de houblon (Humulus lupulus, Cannabinacees). Agressologie (1969 Sep-Oct) 10(5):405-10. ISSN: 0002-1148 (Published in French). [No Abstract Available]

Gorissen H **Bellinck** C **Vancraenenbroeck** R **Lontie** R: [Separation and identification of (+)-gallocatechine in hops]. Arch Int Physiol Biochim (1968 Dec) 76(5):932-4. ISSN: 0778-3124 (Published in French). [No Abstract Available].

Wohlfart R **Wurm** G **Hansel** R **Schmidt** H: [Detection of sedative-hypnotic active ingredients in hops. 5. Degradation of bitter acids to 2-methyl-3-buten-2-ol, a hop constituent with sedative-hypnotic activity]. Arch Pharm (Weinheim) (1983) 316(2):132-7. (Published in German). [No Abstract Available]

Registry Numbers: 115-18-4 (3-hydroxy-3-methylbutene)
468-28-0 (lupulon)
469-02-3 (humulon)

Hansel R **Wagener** HH: [Attempts to identify sedative-hypnotic active substances in hops]. Arzneimittelforschung (1967 Jan) 17(1):79-81. ISSN: 0004-4172 (Published in German). [No Abstract Available].

Mannering GJ **Shoeman** JA **Shoeman** DW: Effects of colupulone, a component of hops and brewers yeast, and chromium on glucose tolerance and hepatic cytochrome P450 in nondiabetic and spontaneously diabetic mice. Biochem Biophys Res Commun (1994 May 16) 200(3):1455-62. ISSN: 0006-291X.

Brewers yeast contains factors that increase and decrease glucose tolerance. Hop components (lupulones) that adhere to yeast during the brewing process elicit a variety of biological effects including the induction of hepatic cytochrome P4503A. Colupulone was tested for its effects on glucose tolerance and cytochrome P450. Serum glucose levels 30 min after the injection of glucose were lowered by colupulone in nondiabetic Swiss-Webster mice, elevated in diabetic C57B1/KSJ-db/db mice, and unaffected in nondiabetic C57B1/KSJ+m/+m mice. Colupulone lowered hemoglobin glycation slightly in +m/+m mice but not in db/db mice. The cytochrome P450 system was highly induced by colupulone in both db/db and +m/+m mice. Chromium, which acts in concert with the factor in yeast that enhances glucose tolerance, had little or no effect on the plasma glucose level or the cytochrome P450 system in either +m/+m or db/db mice.

Registry Numbers: 468-27-9 (colupulone)
50-99-7 (Glucose)
7440-47-3 (Chromium)
9035-51-2 (Cytochrome P-450)

Swanston-Flatt SK **Day** C **Flatt** PR **Gould** BJ **Bailey** CJ: Glycaemic effects of traditional European plant treatments for diabetes. Studies in normal and streptozotocin diabetic mice. Diabetes Res (1989 Feb) 10(2):69-73. ISSN: 0265-5985

Twelve plants used for the traditional treatment of diabetes mellitus in northern Europe were studied using normal and streptozotocin diabetic mice to evaluate effects on glucose homeostasis. The plants were administered in the diet (6.25% by weight) and/or as decoctions or infusions in place of drinking water, to coincide with the traditional method of preparation. Treatment for 28 days with preparations of burdock (Arctium lappa), cashew (Anacardium occidentale), dandelion (Taraxacum officinale), elder (Sambucus nigra), fenugreek (Trigonella foenum-graecum), guayusa (Ilex guayusa), hop (Humulus lupulus), nettle (Urtica dioica), cultivated mushroom (Agaricus bisporus), periwinkle (Catharanthus roseus), sage (Salvia officinale), and wild carrot (Daucus carrota) did not affect the parameters of glucose homeostasis examined in normal mice (basal plasma glucose and insulin, glucose tolerance, insulin-induced hypoglycaemia and glycated haemoglobin). After administration of streptozotocin (200 mg/kg) burdock and nettle aggravated the diabetic condition, while cashew, dandelion, elder, fenugreek, hop, periwinkle, sage and wild carrot did not significantly affect the parameters of glucose homeostasis studied (basal glucose and insulin, insulin-induced hypoglycaemia, glycated haemoglobin and pancreatic insulin concentration). Guayusa and mushroom retarded the development of hyperglycaemia in streptozotocin diabetes and reduced the hyperphagia, polydipsia, body weight loss, and glycated haemoglobin. Mushroom also countered the initial reduction in plasma insulin and the reduction in pancreatic insulin concentration, and improved the hypoglycaemic effect of exogenous insulin. These studies suggest the presence of potentially useful antidiabetic agents in guayusa and mushroom.

Mannering GJ **Shoeman** JA **Deloria** LB: Identification of the antibiotic hops component,

colupulone, as an inducer of hepatic cytochrome P-4503A in the mouse. Drug Metab Dispos (1992 Mar-Apr) 20(2):142-7. ISSN: 0090-9556.

A higher level of cytochrome P-450 (P450)-dependent ethylmorphine (EM) N-demethylase activity was observed in hepatic microsomes from mice fed a natural-ingredient diet ("crude diet") than in those from mice fed a semi-purified diet ("purified diet"). This led to the testing of individual ingredients of the crude diet as inducers of the P-450 system. Brewers yeast proved to be the most significant inductive component of the crude diet. Further investigation revealed that hop components (lupulones) absorbed on yeast during the brewing process were responsible for the induction of the P-450 system. The induction of P-450 and several P-450-dependent monooxygenase activities (EM N-demethylation, aniline hydroxylation, benzo[a]pyrene hydroxylation) by colupulone with respect to dose and time course were investigated. The very large increase in EM N-demethylase activity elicited by colupulone suggested that P-4503A had been induced. Western blot technology verified this speculation. Western blot analysis of microsomal protein from mice fed hops, brewers yeast, or the residue of a hexane extract of hops supported the conclusion that all of these substances induced P-4503A. These substances were also relatively good inducers of P-4502B, but not as inductive of this isozyme as the crude diet. This is interpreted to mean that not all of the inductive properties of the crude diet are due to hop components. These studies question the use of crude commercial diets in studies of P-450 systems. They may also challenge some current definitions of "constitutive" and "induced" P-450s.

Registry Numbers: EC 1.5.3.- (Ethylmorphine-N-Demethylase)
468-27-9 (colupulone)
9035-51-2 (Cytochrome P-450)

Shipp EB **Mehigh** CS **Helferich** WG: The effect of colupulone (a HOPS beta-acid) on hepatic cytochrome P- 450 enzymatic activity in the rat. Food Chem Toxicol (1994 Nov) 32(11):1007-14. ISSN: 0278-6915

Colupulone, a component of hops, was examined for its ability to alter rat hepatic cytochrome P-450 enzymatic activity, expression of hepatic cytochrome P-450 mRNA, and in vitro promutagen activation. Colupulone was fed to male Sprague-Dawley rats for 5 days at 0.36% in the modified AIN 76 diet. Three cytochrome P-450 enzymatic activities were measured, and the corresponding steady-state mRNA levels were examined by Northern blot hybridization. Colupulone increased cytochrome P450IIB and P450IIIA steady-state mRNA levels. In vitro promutagen activation was measured in the Ames assay using liver homogenates from each treatment group. Colupulone treatment did not alter the ex vivo cytochrome P-450-mediated activation of aflatoxin B1 or benzo[a]pyrene to their mutagenic forms. The effect of long-term colupulone administration on in vivo cytochrome P-450 enzymatic activity remains to be determined.

Registry Numbers: 11097-69-1 (aroclor 1254)
1434-54-4 (Pregnenolone Carbonitrile)
468-27-9 (colupulone)
50-32-8 (Benzo(a)pyrene)
9035-51-2 (Cytochrome P-450)

Fenselau C **Kelly** S **Salmon** M **Billets** S: The absence of tetrahydrocannabinol from hops.

Food Cosmet Toxicol (1976 Jan) 14(1):35-9. ISSN: 0015-6264. [No Abstract Available].

Fenselau C **Talalay** P: Is oestrogenic activity present in hops? Food Cosmet Toxicol (1973 Aug) 11(4):597-603. ISSN: 0015-6264. [No Abstract Available].

Simpson WJ **Smith** AR: Factors affecting antibacterial activity of hop compounds and their derivatives. J Appl Bacteriol (1992 Apr) 72(4):327-34. ISSN: 0021-8847.

The antibacterial effect of weak acids derived from the hop plant (Humulus lupulus L.) increased with decreasing pH. Analysis of the minimum inhibitory concentration of such compounds against Lactobacillus brevis IFO 3960 over pH 4-7 suggests that undissociated molecules were mainly responsible for inhibition of bacterial growth. The antibacterial activity of trans-isohumulone was ca 20 times greater than that of humulone, 11 times greater than that of colupulone and nine times greater than that of trans-humulinic acid when the degree of ionization was taken into account. Monovalent cations (K+, Na+, NH4+, Rb+, Li+) stimulated antibacterial activity of trans-isohumulone but the effect was smaller than that observed with H+. The response to divalent cations varied: Ca2+ had little effect on antibacterial activity, whereas Mg2+ reduced activity. Lipid materials and beta-cyclodextrin also antagonized the antibacterial action of trans-isohumulone.

Registry Numbers: 468-27-9 (colupulone)
469-02-3 (humulon)

Verschuere M **Sandra** P **David** F: Fractionation by SFE and microcolumn analysis of the essential oil and the bitter principles of hops. J Chromatogr Sci (1992 Oct) 30(10):388-91 ISSN: 0021-9665.

Supercritical fluid extraction (SFE) is evaluated and optimized for the enrichment and fractionation of the essential oil and the bitter principles of hops (Humulus lupulus), both of which contribute to the flavor of beer. Profiles of the essential oil of different hop varieties are compared. The bitter principles, the humulones and lupulones, are analyzed by miniaturized liquid chromatography (micro-LC) and by micellar electrokinetic chromatography (MEKC).

Haas LF: Neurological stamp. Humulus lupulus (hop). J Neurol Neurosurg Psychiatry (1995 Feb) 58(2):152. ISSN: 0022-3050. [No Abstract Available].

Yasukawa K **Takeuchi** M **Takido** M: Humulon, a bitter in the hop, inhibits tumor promotion by 12-O-tetradecanoylphorbol-13-acetate in two-stage carcinogenesis in mouse skin. Oncology (1995 Mar-Apr) 52(2):156-8. ISSN: 0030-2414.

Humulon, one of the bitters in the hop, was isolated from the female flowers of Humulus lupulus. This component has inhibitory activity against 12-O-tetradecanoylphorbol-13-acetate (TPA)-induced inflammation. At 1 mg/mouse, humulon inhibited markedly the tumor-promoting effect of TPA (1 microgram/mouse) on skin tumor formation following initiation with 7,12-dimethylbenz[a]anthracene (50 micrograms/mouse). Furthermore, humulon inhibited arachidonic acid-induced inflammatory ear edema in mice.

Registry Numbers: 16561-29-8 (Tetradecanoylphorbol Acetate)
469-02-3 (humulon)

506-32-1 (Arachidonic Acid)
57-97-6 (9,10-Dimethyl-1,2-benzanthracene)

Langezaal CR **Chandra** A **Scheffer** JJ: Antimicrobial screening of essential oils and extracts of some Humulus lupulus L. cultivars. Pharm Weekbl Sci (1992 Dec 11) 14(6):353-6. ISSN: 0167-6555.

The essential oils as well as solvent extracts of 11 hop cultivars, 1 hop variety and a wild type of hop were screened for their antimicrobial activities using the agar overlay technique. The oils were isolated from the cones of the various hop plants by hydrodistillation, the extracts were obtained by soaking the hop cones in chloroform. The oils and the extracts showed activity against the Gram-positive bacteria (Bacillus subtilis and Staphylococcus aureus) and the fungus (Trichophyton mentagrophytes var. interdigitale), but almost no activity against the Gram-negative bacterium (Escherichia coli) and the yeast (Candida albicans) used in the screening. The peak area percentages of the main volatile components and the contents of the bitter acids of the extracts were determined for all cultivars using chromatographic methods.

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Gerhard U **Linnenbrink** N **Georghiadou** C **Hobi** V: [Vigilance-decreasing effects of 2 plant-derived sedatives]. Schweiz Rundsch Med Prax (1996 Apr 9) 85(15):473-81. ISSN: 0369-8394 (Published in German).

Previous studies on the efficacy of valerian extracts have given occasional hints of possible side effects involving impaired vigilance. Because of the currently insufficient knowledge about potential impairment of vigilance by plant-based sedatives, we have conducted a controlled study to assess the effects of two plant-based sleep remedies in comparison with flunitrazepam and placebo after single oral administration. Aim of the study was to derive recommendations concerning potential hazards in driving or operating machinery. Residual sedative effects (hangover) were examined in four groups of 20 healthy volunteers, receiving either tablets containing valerian and hops or syrup containing valerian only or flunitrazepam or placebo; furthermore, immediate sedative effects of the two plant preparations have been examined in comparison with placebo (three groups of twelve healthy volunteers). The tests included objective measurements of cognitive psychomotor performance as well as subjective questionnaires on well-being. Tolerability was assessed from spontaneous reports of side effects and a verbal inquiry at the end of the tests. We found that objectively measurable impairment of performance on the morning after medication occurred only in the flunitrazepam group, a finding which was even more pronounced in the subjective questionnaires. In addition, 50% of the volunteers in the flunitrazepam group reported mild side effects in the inquiry at the end of the tests, compared with only 10% from the other groups. The subjective perception of sleep quality was improved in all three medication groups, when compared to placebo. Examination of acute effects of the plant remedies 1 to 2 hours after administration revealed no changes in the more important lead variables; however, a very slight impairment of vigilance after taking syrup was statistically significant as well as a retardation in the processing of complex information for the tablets. The subjective perception of effects was more pronounced (shaky legs, feeling less active). In conclusion, the residual sedative effects (hangover) observed in some earlier studies cannot be confirmed for the recommended doses of the two plant-based sleep remedies which we

have examined with respect to vigilance and cognitive performance. On the contrary: our findings show improved subjective self-assessment (more alert, more active, feeling better). Hangover effects on the following morning need not be a cause for concern, which is of particular interest to car drivers; however, a slight impairment of performance during the first few hours after ingestion should be anticipated. Impairment of vigilance on the morning after ingestion of benzodiazepines, frequently reported and confirmed by our results, constitutes a potential hazard. In this situation, plant remedies such as those examined in this study should be considered as viable alternatives.

Kammerer E: [Phytogenic sedatives-hypnotics - does a combination of valerian and hops have a value in the modern drug repertoire?]. Z Arztl Fortbild (Jena) (1993 Apr 12) 87(5):401-6. ISSN: 0044-2178 (Published in German). [No Abstract Available].

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Hops are told to promote sleep; manyfold efforts to detect the soporific principle have been unsuccessful so far. Preliminary pharmacological tests lead to the conclusion that the soporific activity of the exhalation of hops can be explained by its content of 2-methyl-3-butene-2-ol (1) in the volatile fraction. It was found that 1, when given to mice i.p. (0.80 g/kg) produces narcosis for about 8 h; no abnormal behaviour was observed there upon. Due to its water-solubility the concentration of 1 in the essential oil obtained by steam-distillation is low; contrary to that, 1, is enriched in the more volatile fraction of hops.

Registry Numbers: 115-18-4 (3-hydroxy-3-methylbutene)

Bravo L **Cabo** J **Fraile** A **Jimenez** J **Villar** A: [Pharmacodynamic study of the lupulus' (Humulus lupulus L.) tranquilizing action]. Boll Chim Farm (1974 May) 113(5):310-5 ISSN: 0006-6648 (Published in Spanish). [No Abstract Available].

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The essential oils as well as solvent extracts of 11 hop cultivars, 1 hop variety and a wild type of hop were screened for their antimicrobial activities using the agar overlay technique. The oils were isolated from the cones of the various hop plants by hydrodistillation, the extracts were obtained by soaking the hop cones in chloroform. The oils and the extracts showed activity against the Gram-positive bacteria (Bacillus subtilis and Staphylococcus aureus) and the fungus (Trichophyton mentagrophytes var. interdigitale), but almost no activity against the Gram-negative bacterium (Escherichia coli) and the yeast (Candida albicans) used in the screening. The peak area percentages of the main volatile components and the contents of the bitter acids of the extracts were determined for all cultivars using chromatographic methods.

Krivenko VV **Potebnia** GP **Loiko** VV: [Experience in treating digestive organ diseases with medicinal plants]. Opyt lecheniia nekotorykh zabolevanii organov pishchevareniia lekarstvennymi rasteniiami. Vrach Delo (1989 Mar)(3):76-8. ISSN: 0049-6804 (Published in Russian)

Results are reported of treatment of chronic hyposecretory gastritis, chronic hepatocholecystitis and angiocholitis by a herbal complex. The herbal composition included Achillea millefolium, Urtica dioica, Cichorium (aboveground part), Polygonum, Matricaria chamomilla (flowers), Helichrysum arenarium, Calendula (flowers), corn stigmas, Humulus lupulus (racemes) in proportion 3:3:1:1:2:1:1:2:1 respectively. The herbal decoction is to be taken 3 times daily before meals. Diet N 5 (Pevzner scheme) is to be observed.

Various data sheets

In a data sheet from **Plantextrakt** (through **Aston Chemicals**) we read that hops contain hop bitter acid, flavonoids, essential oil, tannins. It is a sedative, in folk medicine for the treatment of broken skin.

In a data sheet from **Bio-Botanica** (through **Adina**) we read that hops flowers contain a volatile oil consisting mainly of humulene, bitter principles and tannins. Hops is sedative, hypnotic, bactericidal. Has been used on crural ulcers. Will give body to hair, useful in the treatment of ringworm, dandruff, sores, tetters and discolourations.

In a data sheet from **Maruzen Pharmaceuticals** (though **K&K Greeff**) we read that the strobiles are used to produce an extract that is astringent, germicidal, antiphlogistic and disinfectant.

In a data sheet from **Haarman and Reimer** we read that hops are *Humulus lupulus* and that the cone is used. It is grown mainly in Germany, the United States and China. It is sedative, promotes wound healing and is antiphlogistic.

It contains chlorogenic acid, hyperosid, rutin and quercetin. The amino acids detectable are asparagine, alanine, arginine, valine, serine, isoleucine, glycine.

In a botanical information sheet from **A.Webster** of **English Grains** we read that the strobiles of the hops are used, to some extent hops glandulae. They contain essentail oil, humulons, lupulons (α- and ß-acids); 2-methyl-3-buten-ole; more than 150 constituents are known.

It is calming, sleep inducing. 2-methyl-3-buten-ole, split off from humulons and lupulons, is supposed to have a high sedative effect. The splitting takes place during storage of the drug or extract, but also after ingestion of the medicine. Hops is used in treatments of various feelings of ill health such as unrest, anxiety states and sleep disturbances.

Hops has often been applied as tincture for the topical treatment of ulcers and broken skin; internal application in case of cystitis. Hops is used as a bitter tonic or tea and as stomachic to induce appetite and stimulate gastric secretion.

INTERNET DATA

HOPS

Synonyms: Humulus, Lupulus

Family: Cannabinaceae or Moraceae

Genus species: *Humulus lupulus*

Type: Dioecious perennial climbing herb

Part Used: Strobiles from female plant

Location: China, India, Temperate Zones, U.S., Western Europe

Actions: Anaphrodisiac, anodyne, antimicrobial, antiseptic (topical), antispasmodic (on smooth muscles esp. intestines), antituberculotic, appetite stimulant, aromatic bitter, astringent, bactericide, bactericide (topical), bitter, calmative, decreases the desire for

alcohol, diuretic, expectorant, hepatic, hypnotic, mild depressant, nervine, possible action against cysts and cancer, respiratory stimulant, sedative, soporific, spasmolytic, stomachic, tonic, vermifuge

Indications: Acidosis, anorexia, anxiety, cirrhosis, Crohn's disease, cystitis, dyspepsia, dysuria, earache, excitability, fever, gonorrhea, hyperexcitability, indigestion, inflammation, insomnia, irritable bowel syndrome, leg ulcers (topical), migraine, mucous colitis, muscle spasms, nervous insomnia, nervous restlessness, neuralgia, pain, poor circulation, priapism, rheumatism, spastic colon, stress, tension headache, toothache, trigeminal neuralgia, tuberculosis, ulcer, urethritis

Chemicals & Nutrients: Calcium, Carbohydrates (77%), Fats (3%), Fiber (7%), Fructose, Glucose, Magnesium, Pectin, Phosphorus, Potassium, Protein (18%), Vitamin C

Preparation & Dosages:
Dried strobile: dose 0.5-1 g
Hypnotic: 1-2 g, or by infusion
Liquid extract: 1:1 in 45% alcohol, dose 0.5-2 ml
Pillow filled with hops will induce sleep
Tincture: 1:5 in 60% alcohol, dose 1-2 ml

Contraindications: Inadvisable in depression.
Drug interactions: Combinations with other sedative drugs may be advantageous.

Note: Fresh hops are best since potency is rapidly lost during storage.

Safety: GRAS.