



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

6 May 2014
EMA/HMPC/682386/2013
Committee on Herbal Medicinal Products (HMPC)

List of references supporting the assessment of *Humulus lupulus* L., flos

Final

The European Medicines Agency acknowledges that copies of the underlying works used to produce this monograph were provided for research only with exclusion of any commercial purpose.

Anonymous. *Humulus lupulus*. Monograph. *Alternat Med Rev* 2003a; 8(2): 190-192.

Anonymous. Harvard Medical School, 2003b.

Belgian legislation on herbals: MB 25/02/2005.

Blumenthal M, Goldberg A, Brinckmann J, editors. Herbal medicine: Expanded commission E monographs, first ed. Integr Med Comm, Newton 2000, 193-196.

Brattström A. Scientific evidence for a fixed extract combination (Ze 91019) from valerian and hops traditionally used as a sleep-induced aid. *Wien Med Wochenschr* 2007, 157 (13-14): 367-370.

Brattström A. Wirksamkeitsnachweis von Phytopharmaka am Beispiel einer Hopfen-Baldrian-Kombination. *Forsch Komplementärmed* 1996, 3: 188-195.

Bravo L, Cabo J, Fraile A, Jimenez J, Villas A. Estudio farmacodinamico del lupulo (*Humulus lupulus* L.) action tranquilizante. *Bull Chim Farm* 1974, 113: 310-315.

British Herbal Pharmacopoeia. *Humulus*. British Herbal Medicine Association, London, 1983, 111-112.

Butterweck V, Brattström A, Grundmann O, Koetter U. Hypothermic effects of hops are antagonized with the competitive melatonin receptor antagonist luzindole in mice. *J Pharm Pharmacol* 2007, 59: 549-552.

Casaschi A, Maiyoh GK, Rubio BK, Li RW, Adeli K, Theriault AG. The chalcone xanthohumol inhibits triglyceride and apolipoprotein B secretion in HepG2 cells. *J Nutrition* 2004, 134 (6): 1340-1346.

Caujolle F, Pham Huu Chanh, Duch-Kan P, Bravo Diaz L. Etude de l'action spasmodolytique du houblon (*Humulus lupulus*, Cannabinacées). *Agressologie* 1969, 10: 405-410.



- Chadwick LR, Pauli GF, Farnsworth NR. The pharmacognosy of *Humulus lupulus* L. (hops) with the emphasis on estrogenic properties. *Phytomedicine* 2006, 13(1-2): 119-131.
- Christoffel J, Rimoldi G, Wuttke W. Effects of 8-prenylnaringenin on the hypothalamo-pituitary-uterine axis in rats after 3-month treatment. *J Endocrinol* 2006, 188(3): 397-405.
- Coldham NG, Horton R, Byford MF, Sauer MJ. A binary screening assay for pro-estrogens in food: metabolic activation using hepatic microsomes and detection with oestrogen sensitive recombinant yeast cells. *Food Addit Contam* 2002, 19: 1138-1147.
- Coldham NG, Sauer MJ. Identification, quantitation and biological activity of phytoestrogens in a dietary supplement for breast enhancement. *Food Chem Toxicol* 2001, 39: 1211-1224.
- Cornu C, Remontet ML, Noel-Baron F, Nicolas A, Feugier-Favier N, Roy P, Claustrat B., Saadation-Elahi M, Kassai B. A dietary supplement to improve the quality of sleep: a randomized placebo controlled trial, *BMC Complem Altern M* 2010, 10: 29-39.
- Deutsches Arzneibuch, DAB 10, 1991.
- De Cooman L, Everaert E, De Keukeleire D. Quantitative analysis of hop acids, essential oils and flavonoids as a clue to the identification of hop varieties. *Phytochem Anal* 1998, 9: 145-150.
- Decroos K, Vanhemmens S, Cattoir S, Boon N, Verstraete W. Isolation and characterisation of an equol producing mixed microbial culture from a human faecal sample and its activity under gastrointestinal conditions. *Arch Microbiol* 2005, 183: 45-55.
- De Keukeleire D, De Cooman L, Rong H, Heyerick A., Kalita J, Milligan SR. Functional properties of hop polyphenols. In: Gross GG, Hemingway RW, Yoshida T, editors. *Plant Polyphenols 2: Chemistry, Biology, Pharmacology, Ecology*. New York: Kluwer Academic Plenum Publishers, 1999: 739-760.
- De Keukeleire D, Milligan SR, De Cooman L, Heyerick A. The oestrogenic activity of hops (*Humulus lupulus* L.) revisited. *Pharm Pharmacol Lett* 1997; (2-3): 83-86.
- De Keukeleire D, Heyerick A, Prenylflavonoids account for intriguing biological activities of hops; Proc. 1st IS on Humulus, Eds. Hummer KE and Henning JH, Acta Hort 668, ISHS, 2005.
- Diel P, Thomae RB, Caldarelli A, Zierau O, Kolba S, Schmidt S, Schwab P, Metz P, Vollmer G. Regulation of gene expression by 8-prenylnaringenin in uterus and liver of Wistar rats. *Planta Med* 2004, 70: 39-44.
- Dietz B, Kung YH, Liu G, Eggler AL, Yao P, Chadwick LR, Pauli GF, Farnsworth NR, De Mesear RB, van Breemen RB, Bolton JL. Xanthohumol isolated from *Humulus lupulus* inhibits menadion-induced DNA damage through induction of quinone-reductase. *Chem Res Tox* 2005, 18: 1296-1305.
- Dixon-Shanies D, Shaikh N. Growth inhibition of human breast cancer cells by herbs and phytoestrogens. *Oncol Rep* 1999, 6: 1383-1387.
- Dorn C, Weiss TS, Heilmann J, Hellerbrand C. Xanthohumol, a prenylated chalcone derived from hops, inhibits proliferation, migration and interleukine-8 expression of hepatocellular carcinoma cells, *Int J Oncology* 2010, 36: 435-441.
- Effenberger KE, Johnson SA, Monroe DG, Spelsberg TC, Weestendorf JJ. Regulation of osteoblastic phenotype and gene expression by hop derived phytoestrogens. *J Ster Biochem Mol Biol* 2005, 96 : 387-399.

- Eri S, Khoo BK, Lech J, Hartman TG. Direct thermal desorption gas chromatography and gas chromatography mass spectrometry profiling of hop (*Humulus lupulus* L.) essential oils in support of varietal characterization. *J Agric Food Chem* 2000, 48: 1140-1149.
- Erkolla R, Vervarcke S, Hurskainen P, Heyerick A, De Keukeleire D. A randomized, double-blind, cross-over study on the use of a standardized hop extract to alleviate menopausal discomforts. *Phytomedicine* 2010, 17: 389-326.
- ESCOP Monographs Second Ed., Thieme Verlag, 2003, 306-311.
- Estrada J, Gozala F, Cecchini L, Casquette E. Contact urticaria from hops (*Humulus lupulus*) in a patient with previous urticaria-angioedema from peanut, chestnut, and banana. *Contact Dermat* 2002, 46: 127.
- European Pharmacopoeia , 5th Ed., Council of Europe. Lupuli flos 01/2005:1222
- Fenselau C, Talahay P. Is oestrogenic activity present in hops? *Food Cosmet Toxicol* 1973, 11: 597-603.
- Finn CA, Publicover M. Hormonal control of cell death in the luminal epithelium of the mouse uterus. *J Endocrin* 1981, 91: 335-340.
- Fintelmann V, Menssen HG, Siegers CP. Phytotherapie Manual, 2 Vol, Hippocrates Verlag, Stuttgart, 1993: 113-114.
- Flesch P. Hopfen-Baldrian-Kombination als Benzodiazepin-Ersatz? *Geriatric Praxis* 1997, (21-23).
- Franco L, Sanchez C, Rodriguez AB, Baariga C, Romero RE. The sedative effect of non-alcoholic beer in healthy female nurses, *PLOS one* 2012a, 7(7): 1-6.
- Franco I, Sanchez C, Bravo R, Rodriguez A, Barriga C, Cubero JC. The sedative effect of hops (*Humulus lupulus*), a component of beer, on the activity rest rhythm. *Acta Physiologica Hungara* 2012b, 99: 33-139.
- Füssel A, Wulf A, Brattström, A. Effect of a fixed valerian-hop extract combination (ZE91019) on sleep polygraphy in patients with non-organic insomnia: a pilot study. *Eur J Med Res* 2000, 18(5): 385-390.
- Gerhauser C, Alt A, Eldeen AG, Neumann I, Frank N, Chmiel H, Bartsch H, Becker H. Antioxidant and radical-scavenging potential of phenolic constituents of beer. *Proc Am Assoc Cancer Res* 2001b, 42: 18.
- Gerhauser C, Alt A, Heiss E, et al. Cancer chemopreventive activity of xanthohumol, a natural product derived from hop. *Mol Cancer Ther* 2002, 1: 959-969.
- Gerhauser C, Frank N. Xanthohumol, a new all-rounder? *Molec Nutr & Food Res* 2005, 49(9):821-823.
- Göggelmann W, Schimmer O. Mutagenic activity of phytotherapeutical drugs. In: Knudsen I, editor. Genetic Toxicology of the Diet. New York : Alan R. Liss, 1986; 63: 72.
- Goetz P. Traitement des bouffées de chaleur par insuffisance ovarienne par l'extract de houblon (*Humulus lupulus*). *Revue de Phytoth Prat* 1990, 4: 13-15.
- Grès MC, Julian B, Bourrié M, Meunier V, Roques C, Berger M, Boulenc X, Berger Y, Fabre G. Correlation between oral drug absorption in humans and apparent drug permeability in TC-7 cells, a human epithelial intestinal cell line: comparison with the parental Caco-2 cell line. *Pharm Res* 1998, 15: 726-733.

- Grundmann O, Brattström A, Koetzer U, Butterweck V. Hypothermic effects of hops could antagonise with the competitive melatonin receptor antagonist luzindole. *Planta Med* 2006, (11): 1065, 281.
- Guo J, Nikolic D, Chadwick LR, Pauli GF, van Breemen RB. Identification of human hepatic cytochrome P450 enzymes involved in the metabolism of 8-prenylnaringenin and isoxanthohumol from hops (*Humulus lupulus* L.). *Drug Metab Dispos* 2006, 34 (7): 1152-1159.
- Hagers Handbuch der Pharmazeutische Praxis, Hrsg. Hänsel R, Keller K, Rimpler H, Schneider G, Springer Verlag 1993: 447-458.
- Hänsel R, Schulz J. Hopfen und Hopfenpräparate: Fragen zur pharmazeutischen Qualität. *Dtsch Apoth Ztg* 1986; 126: 2033-2037.
- Hänsel R, Wagener HH. Versuche, sedative-hypnotische Wirkstoffe in Hopfen nachzuweisen. *Arzneim-Forsch/Drug Res* 1967, 17: 79-81.
- Hänsel R, Wohlfart R, Coper H. Versuche, sedativ-hypnotische Wirkstoffe im Hopfen nachzuweisen. II. Narcotic action of 2-methyl-3-butene-2-ol, contained in the exhalation of hops. *Z Naturforsch* 1980; 35c: 1096-1097.
- Hänsel R, Wohlfart R, Schmidt H. Nachweis sedativ-hypnotischer Wirkstoffe im Hopfen. 3. Mitteilung: Der Gehalt von Hopfen und Hopfenzubereitungen an 2-Methyl-3-buten-2-ol. *Planta Med* 1982, 45: 224-228.
- Henderson MC, Miranda CL, Stevens JF, Deinzer ML, Buhler DR. *In vitro* inhibition of human P450 enzymes by prenylated flavonoids from hops, *Humulus lupulus*. *Xenobiotica* 2000, 30: 235-251.
- Heyerick A, Vervarcke S, Depypere H, Bracke M, De Keukeleire D. A first prospective, randomized, double-blind placebo-controlled study on the use of a standardized hop extract to alleviate menopausal discomfort. *Maturitas* 2006, 54: 169-175.
- Hölz J. Inhaltsstoffe des Hopfens (*Humulus lupulus* L.). *Z Phytother* 1992, 13: 155-161.
- Hümpel M, Isaksson P, Schaefer O, Kaufmann U, Ciana P, Maggi A, Schleuning WD. Tissue specificity of 8-prenylnaringenin : Protection from ovariectomy induced bone loss with minimal trophic effects on the uterus. *J Steroid Biochem Mol Biol* 2005, 97: 299-305.
- Kitaoka M, Kadokawa H, Sugano M, Ichikawa K, Taki M, Takaishi S et al. Prenylflavonoids : a new class of non-steroidal phytoestrogens (Part 1). Isolation of 8-isopentenylaringenin and an initial study on its structure-activity relationship. *Planta Med* 1998, 64: 511-515.
- Koch W, Heim G. Östrogene hormone in Hopfen und Bier. *Münch Med Wochenschr* 1953, 95: 845.
- Koetter U, Schrader E, Käufeler R, Brattström A. A randomized, double-blind, placebo-controlled, prospective clinical study to demonstrate clinical efficacy of a fixed valerian hops extract combination (Ze 91019) in patients suffering from non-organic sleep disorder. *Phytother Res* 2007, 21: 847-851.
- Kumai A, Okamoto R. Extraction of the hormonal substance from hops. *Toxicol Lett* 1984, 21: 203-207.
- Lataster MJ, Brattström A. Die Behandlung von Patienten mit Schlafstörungen. Wirksamkeit und Verträglichkeit von Baldrian-Hopfen-Dragees. *Notabene Medici* 1996, 4: 182-185.
- Laughlin ,GA, Barrett-Conner E, Criqui MH, Kritz-Silverstein D. The prospective association of serum insuline-like growth factor I(IGF-I) and IGF-binding protein-1 levels with all cause and cardiovascular

diseases mortality in older adults: the Rancho Bernardo Study. *J Clin Endocrinol Metabol* 2004, 89: 114-120.

Leathwood PD, Chauffard F, Heck E, Munoz-Box R. Aqueous extracts of valerian root (*Valeriana officinalis* L.) improves sleep quality in man. *Pharmacol Biochem Behav* 1982, 17: 67-71.

Lee KM, Jung JS, Song DK, Krauter M, Kim YH. Neuropharmacological activity of *Humulus lupulus* extracts. *Korean J Pharmacogn* 1993b, 24:231-234.

Lee KM, Song DK, Krauter M, Kim YH. Neurological activity of *Humulus lupulus* extract on the central nervous system in mice. *Planta Med* 1993a, 59:A691.

Lee YM, Hsieh KH, Lu WJ, Chou HC, Chou DS, Lien L.M, Sheu JR, Lin KH. Xanthohumol, a prenylated flavonoid from hops (*Humulus lupulus*), prevents platelet activation in human platelets, *Evid-Based Compl Alt* 2012, Article ID 852362.

Liu J, Burdette JE, Xu H, Gu C, van Breemen RB, Bhat KP, Booth N, Constantinou AI, Pezzuto JM, Fong HHS, Farnsworth NR, Bolton JL. Evaluation of estrogenic activity of plant extracts for the potential treatment of menopausal symptoms. *J Agric Food Chem* 2001, 49: 2472-2479.

McMurrough I. High performance liquid chromatography of flavonoids in barley and hops. *J Chromatogr* 1981, 316: 132-137.

Meissner O, Häberlein H. Influence of xanthohumol on binding behaviour of GABA_A receptors and their lateral mobility at hippocampal neurons. *Planta Medica* 2006, 72: 656-68.

Milligan S, Kalita J, Pocock V, Heyerick A, De Cooman L, Rong H, De Keukeleire D. Oestrogenic activity of the hop phyto-oestrogen, 8-prenylnaringenin. *Reproduction* 2002, 123: 235-242.

Milligan SR, Kalita JC, Heyerick A, Rong H, De Cooman L, De Keukeleire D. Identification of a potent phytoestrogen in hops (*Humulus lupulus* L.) and beer. *J Clin Endocrinol Metab* 1999, 84: 2249-2252.

Milligan SR, Kalita JC, Pocock V, Van De Kauter V, Stevens JF, Deinzer ML, Rong H, De Keukeleire D. The endocrine activities of 8-prenylnaringenin and related hop (*Humulus lupulus* L.) flavonoids. *J Clin Endocrinol Metab* 2000, 85: 4912-4915.

Miranda CL, Stevens JF, Ivanov V, McCall M, Frei B, Deinzer ML, Buhler DR. Antioxidant and prooxidant actions of prenylated and nonprenyated chalcones and flavanones *in vitro*. *J Agric Food Chem* 2000c; 48: 3876-3884.

Miranda CL, Yang YHA, Henderson MC, Rodriguez RJ, Yang Y-H, Deinzer ML, Barnes DW, Buhler DR. Prenylflavonoids from hops inhibit the metabolic activation of the carcinogenic heterocyclic amine 2-amino-3-methylimidazo (4,5-F) quinoline, mediated by cDNA-expressed human CYP1A2. *Drug Metab Disp* 2000a, 28: 1297-1302.

Miyamoto M, Matsushita Y, Kiyokawa A, Fukuda C, Iijima Y, Sugano M, Akiyama T. Prenylflavonoids: a new class of non-steroidal phytoestrogen (part 2). Estrogenic effects of 8-isopentenylaringenin on bone metabolism. *Planta Med* 1998; 64: 516-519.

Morali G, Polatti F, Metilitser EN, Mascarucci P, Magnani P, Marzè PB. Open, non-controlled clinical studies to assess the efficacy and safety of a medical device in form of gel topically and intravaginally used in postmenopausal women with genital atrophy. *Arzneimittelforsch* 2006, 56(3): 230-238.

Morin CM, Koetter U, Bastien C, Wane JC, Wooter V. Valerian-hops combination and diphenhydramine for treating insomnia : a randomised placebo-controlled clinical trial. *Sleep* 2005, 28(11): 1465-1471.

Mueller-Limmroth W, Ehrenstein W. Experimental studies of the effects of Seda-Kneipp on the sleep of sleep disturbed subjects: implications of the treatment of different sleep disturbances. *Med Klin* 1977, 72: 1119-1125.

Newal CA, Anderson LA, Phillipson JD. Hops Herbal Medicines. A guide for healthcare professionals. 1st Ed. Pharmaceutical Press, London, Chicago 1996: 162-163.

Newark FM. Hops allergy and terpene sensitivity: an occurred disease. *Am Allergy* 1978, 41:311-312

Ngo TH, Barnard RJ, Leung PS, Cohen P, Aronson WJ. Insulin-like growth factor I (IGF-I) and IGF-binding protein-1 modulate prostate cancer cell growth and apoptosis: Possible mediators for the effects of diet and exercise on cancer cell survival. *Endocrinology* 2003, 144: 2319-2324.

Nikolic D, Li Y, Chadwick LR, Grubjesic S, Schwab P, Metz P, van Breemen RB. Metabolism of 8-prenylnaringenin, a potent phytoestrogen from hops (*Humulus lupulus* L.), by human liver microsomes. *Drug Metab Dispos* 2004, 32: 272-279.

Nikolic D, Li Y, Chadwick LR, Pauli GF, van Breemen RB. Metabolism of xanthohumol and isoxanthohumol, prenylated flavonoids from hops (*Humulus lupulus* L.), by human liver microsomes. *J Mass Spectrom* 2005, 40: 289-299.

Nikolic D, Li Y, Chadwick LR, van Breemen RB. *In vitro* studies of intestinal permeability and hepatic and intestinal metabolism of 8-prenylnaringenin, a potent phytoestrogen from hops (*Humulus lupulus* L.). *Pharm Res* 2006; 23, (5): 864-872.

Notter D, Brattström A, Morandell D, Polasek W. Wirksamkeit und Sicherheit eines Baldrian-Hopfen-Kombinationspräparates bei verschiedenen Schlafstörungen. *Phytotherapie* 2003; 3: 9-12.

Overk CR, Yao P, Chadwick LR, Nikolic D, Sun YK, Cuendet MA, Deng YF, Hedayatt AS, Pauli GF, Farnworth NR, van Breemen RB, Bolton JL. Comparison of the *in vitro* estrogenic activities of compounds from hops (*Humulus lupulus*) and red clover (*Trifolium pratense*). *J Agric Food Chem* 2005, 53: 6246-6253.

Pepper MS, Hazel SJ, Hümpel M, Schleuning W-D. 8-Prenylnaringenin, a novel phytoestrogen inhibits angiogenesis *in vitro* and *in vivo*. *J Cell Physiol* 2004, 199: 98-107.

Pharmacopée Française, 10^{me} Ed. Houblon, *Humulus lupulus*, 1989.

Possemiers S, Bolca S, Grootaert C, Heyerick A, Decroos K, Dhooge W, De Keukeleire D, Rabot S, Verstraete W, Van de Wiele T. The prenylflavonoid isoxanthohumol from hops (*Humulus lupulus* L.) is activated into the potent phytoestrogen 8-prenylnaringenin *in vitro* and in the human intestine. *J Nutr* 2006, 136 (7): 1862-1867.

Possemiers S, Heyerick A, Robbens V, De Keukeleire D, Verstraete W. Activation of proestrogens from hops (*Humulus lupulus* L.) by intestinal microbiota. Conversion of isoxanthohumol into 8-prenylnaringenin. *J Agricul and Food Chem* 2005, 53: 6281-6288.

Rad M, Hümpel M, Schaefer O, Schoemaker RC, Schleuning WD, Cohen AF, Burggraaf S. Pharmacokinetics and systemic endocrine effects of the phyto-oestrogen 8-prenylnaringenin after single oral doses to postmenopausal women. *Br J Cl Pharm* 2006, 62(3): 288-296.

Rodenbeck A, Hajak G. Polysomnographische Pilotstudie zur Wirkung von Hopfen/Baldrian auf den Schlaf von Patienten mit primärer Insomnie. Eine doppelblinde, randomisierte, placebokontrollierte Studie im Schlaflabor, 1998, Study Report MI 9221.

- Rong H, Boterberg T, Maubach J, Stove C, Depypere H, Van Slambrouck S, Serreyn R, De Keukeleire D, Marlee M, Bracke M. 8-Prenylnaringenin, the phytoestrogen in hops and beer, upregulates the function of the E-cadherin-catenin complex in human mammary carcinoma cells. *Eur J Cell Biol* 2001, 80: 580-585.
- Rong H, Zhao Y, Laou K, De Keukeleire D, Milligan SR, Sandra P. Quantitation of 8-prenylnaringenin, a novel phytoestrogen in hops (*Humulus lupulus* L.), hop products and beers, by HPLC-MS using atmospheric pressure electrospray ionization. *Chromatographia* 2000, 51: 545-552.
- Rowland I, Faughnan M, Hoey L, Wahala K, Williamson G, Cassidy A. Bioavailability of phytoestrogens. *Br J Nutr* 2003, 89: 45-58.
- Schaefer O, Hümpel M, Fritzemeier KH, Bohlmann R, Schleuning WD. 8-Prenylnaringenin is a potent ER alpha selective phytoestrogen present in hops and beer. *J Steroid Biochem and Mol Biol* 2003, 84: 359-360.
- Schaefer O. Untersuchungen zum Phytoestrogen 8-prenylnaringenin aus Hopfen für den Einsatz in der Hormon-Ersatz-Therapie. Universität Hannover, Ph D Thesis, 2004.
- Schellenberg A, Sauer S, Abourashed EA, Koetter U, Brattström A. The fixed combination of valerian and hops (Ze91019) acts via a central adenosine mechanism. *Planta Med* 2004, 70: 694-697.
- Schiller H, Forsten A, Vonhoff C, Hegger M, Biller A, Wintershoff H. Sedating effects of *Humulus lupulus* L. extracts. *Phytomedicine* 2006; 13: 535-541.
- Schmitz M, Jäckel M. Comparative study for assessing quality of life of patients with exogenous sleep disorders (temporary sleep onset and sleep interruption disorders) treated with a hops-valerian preparation and a benzodiazepine drug. *Wien Med Wochenschr* 1998, 148: 291-298.
- Schulz J, Hänsel R, Tyler VE. Hop strobiles and hop glands. In: Rational Phytotherapy. Springer, Berlin, Germany, 2001.
- Shimamura M, Hazato T, Ashino H, Yamamoto Y, Iwasaki E, Tobe H, Yamamoto K, Yamamoto S. Inhibition of angiogenesis by humulone, a bitter acid from beer hop. *Biochem Biophys Res Commun* 2001, 289: 220-224.
- Stevens JF, Ivančić M, Hsu VL, Deinzer ML. Prenylflavonoids from *Humulus lupulus*. *Phytochem* 1997, 44: 1575-1585.
- Stevens JF, Page JE. Xanthohumol and related prenylflavonoids from hops and beer: to your good health. *Phytochem* 2004, 65: 1317-1330.
- Stevens JF, Taylor AW, Clawson JE, Deinzer ML. Fate of xanthohumol and related prenylflavonoids from hops to beer. *J Agric Food Chem* 1999a, 47: 2421-2428.
- Stevens JF, Taylor AW, Deinzer ML. Quantitative analysis of xanthohumol and related prenylflavonoids in hops and beer by liquid chromatography-tandem mass spectrometry. *J Chromatogr A* 1999b, 832: 97-107.
- Tobe H, Kubota M, Yamaguchi M, Kocka T, Aoyagi T. Apoptosis to HL-60 by humulone. *Biosci Biotechnol Biochem* 1997b, 61: 1027-1029.
- Tokalov SV, Henker Y, Schwab P, Metz P, Gutzeit HO. Toxicity and cell cycle effects of synthetic 8-prenylnaringenin and derivatives in human cells. *Pharmacology* 2004, 71: 46-56.

- Turner NJ, Thomson BM, Shaw IC. Bioactive isoflavones in functional foods: The importance of gut microflora on bioavailability. *Nutr Rev* 2003, 61: 204-213.
- Van hoecke B, Derycke L, Van Marck V, Depypere H, De Keukeleire D, Bracke M. Anti-invasive effect of xanthohumol, a prenylated chalcone present in hops (*Humulus lupulus* L.) and beer. *Intern J Cancer* 2005, 117(6): 889-895.
- Verzele M. Centenary review: 100 years of hop chemistry and its relevance to brewing. *J Inst Brew* 1986, 92: 32-48.
- Wegener T. Phytopharmaka zur Anxiolyse. Zur Wirkung einer Kombination von Baldrian und Hopfen bei Angstzuständen. *Dt Apoth Ztg* 2003, 143: 618-625.
- Wichtl M. Teedrogen, Vol 2, Wissenschaftliche Verlagsgesellschaft übH, Stuttgart, 1989, 242-245.
- Wohlfart R, Hänsel R, Schmidt H. Nachweis sedativ-hypnotischer Wirkstoffe im Hopfen. Mitteilung: Die Pharmakologie des Hopfeninhaltsstoffe 2-Methyl-3-buten-2-ol. *Planta Med* 1983a, 48: 120-123.
- Wohlfart R, Wurm G, Hänsel R, Schmidt H. Nachweis sedativ-hypnotischer Wirkstoffe im Hopfen. 5. Mitteilung: Der Abbau der Bittersäuren zum 2-Methyl-3-buten-2-ol, einem Hopfeninhaltsstoff mit sedativ-hypnotischer Wirkung. *Arch Pharm (Weinheim)* 1983b, 316: 132-137.
- Wohlfart R. Humulus. In: Hänsel R, Keller K, Rimpler H, Schneider G, editors. Hagers Handbuch der pharmazeutischen Praxis, 5th ed. Volume 5, Drogen E-O. Berlin: Springer-Verlag, 1993: 447-458.
- Wohlfart R. Wirkstoffprobleme des Hopfens. *Z Phytotherapie* 1982, 3: 393-395.
- Yilmazer M, Stevens JF, Deinzer ML, Buhler DR. *In vitro* biotransformation of xanthohumol, a flavonoid from hops (*Humulus lupulus*), by rat liver microsomes. *Drug Metab Dispos* 2001a, 29: 223-231.
- Zanoli P, Rivasi M, Zavatti M, Brusiani F, Bardhi M. New insight in the neuropharmacological activity of *Humulus lupulus* L. *J Ethnopharmacol* 2005, 102: 102-106.
- Zhang N, Liu Z, Han Q, Chen J, Lv Y. Xanthohumol enhances antiviral effect of interferon alfa-2b against bovine viral diarrhoea virus, a surrogate of hepatitis C virus. *Phytomedicine* 2010, 17: 310-317.
- Zierau O, Gester S, Schwab P, Metz P, Kolba S, Wulf M, Vollmer G. Estrogenic activity of the phytoestrogens naringenin, 6-(1,1-dimethylallyl)naringenin and 8-prenylnaringenin. *Planta Med* 2002, 68: 449-451.
- Zierau O, Hamonn J, Tischer S, Schwab P, Metz P, Vollmer G, Gutzeit HO, Scholz S. Naringenin-type flavonoids show different estrogenic effects in mammalian and teleost test systems. *Biochem Biophys Res Commun* 2005, 326: 909-916.
- Zierau O, Hauswald S, Schwab P, Metz P, Vollmer G. Two major metabolites of 8-prenylnaringenin are estrogenic *in vitro*. *J Steroid Biochem and Molec Biol* 2004, 92: 107-110.
- Zierau O, Morissey C, Watson RWG, Schwab P, Kolla S, Metz P, Vollmer G. Antiandrogenic activity of the phytoestrogens naringenin, 6-(1,1-dimethylnaringenin) and 8-prenylnaringenin. *Planta Med* 2003, 69: 856-858.