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# Lemon Balm

Updated: February 10, 2024.

# **OVERVIEW**

# Introduction

Lemon balm is an oily extract of the leaves of Melissa officinalis, a flowering perennial shrub native to the east Mediterranean and west Asian regions that is now cultivated widely. Lemon balm was used in traditional medicine for nervousness, anxiety, insomnia, and menstrual irregularities. Lemon balm extracts are generally recognized as safe and have not been linked to serum aminotransferase elevations during treatment or to instances of clinically apparent acute liver injury.

## Background

Lemon balm is an extract made from the fresh or dried leaves of Melissa officialis, a moderate sized, flowering shrub native to the eastern Mediterranean area and western Asia but now cultivated in many areas of the world. Lemon balm extracts contain aromatic, lemony smelling oils, chief of which are citronellal and geranial. Lemon balm also contains glycosides, caffeic acid derivatives, flavonoids, and triterpene acids. Lemon balm has mild sedative and antispasmodic activities in vitro. Melissa officialis is often included in multiingredient products used to alleviate gastrointestinal symptoms, anxiety, and psychological conditions including depression. Lemon Balm extract is generally well tolerated and has few if any adverse events.

#### Hepatotoxicity

Lemon balm extract has not been linked to serum enzyme elevations during therapy, although there have been few prospective studies in humans that have reported on laboratory test results during treatment. In small trials, lemon balm extracts have appeared to be well tolerated with only a few minor adverse non-specific effects (headache, dizziness, bloating), which often have been similar in frequency among persons receiving placebo. Despite widescale use as an herbal supplement, lemon balm extract has not been linked to published instances of clinically apparent liver injury. Lemon balm extracts are often included in multiingredient dietary supplements some of which have been implicated in liver injury, but a specific contribution from lemon balm to the injury could not be established. The frequency of hypersensitivity reactions to lemon balm extract is also not known.

Likelihood score: E (unlikely cause of clinically apparent liver injury).

Other Names: Balm, Common Balm, Honey Plant, Sweet Balm, Sweet Mary, Melissa.

Drug Class: Herbal and Dietary Supplements

# **PRODUCT INFORMATION**

**REPRESENTATIVE TRADE NAMES** 

Lemon Balm – Generic

DRUG CLASS

Herbal and Dietary Supplements

# **CHEMICAL FORMULA AND STRUCTURE**

DRUG	CAS REGISTRY NUMBER	MOLECULAR FORMULA	STRUCTURE
Citronellal	106-23-0	С10-Н18-О	SID: 134971626

## **ANNOTATED BIBLIOGRAPHY**

References updated: 10 February 2024

Abbreviations: DSHEA, Dietary Supplement Health and Education Act; HDS, herbal and dietary supplements.

- Zimmerman HJ. Unconventional drugs. Miscellaneous drugs and diagnostic chemicals. In, Zimmerman, HJ. Hepatotoxicity: the adverse effects of drugs and other chemicals on the liver. 2nd ed. Philadelphia: Lippincott,1999: pp. 731-4.
- (*Expert review of hepatotoxicity published in 1999; several herbal medications linked to liver injury are discussed, but lemon balm is not mentioned*).
- Seeff L, Stickel F, Navarro VJ. Hepatotoxicity of herbals and dietary supplements. In, Kaplowitz N, DeLeve LD, eds. Drug-induced liver disease. 3rd ed. Amsterdam: Elsevier, 2013, pp. 631-58.
- (Review of hepatotoxicity of herbals does not mention lemon balm).
- Lemon Balm (*Melissa officinalis*). PDR for Herbal Medicines. 4th ed. Montvale, New Jersey: Thomson Healthcare Inc. 2007: pp 514-5.
- (Compilation of short monographs on herbal medications and dietary supplements).
- Electronic Code of Federal Regulations. Title 21. Part 182. Substances Generally Recognized As Safe. Available at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=182
- (Listing of botanical and herbal products that are "generally recognized as safe" (GRAS) according to FDA criteria, which permits them to be sold as over-the-counter supplements without prior proof of safety and efficacy).
- Russo MW, Galanko JA, Shrestha R, Fried MW, Watkins P. Liver transplantation for acute liver failure from drug-induced liver injury in the United States. Liver Transpl 2004; 10: 1018-23. PubMed PMID: 15390328.
- (Among ~50,000 liver transplants reported to UNOS between 1990 and 2002, 270 [0.5%] were done for drug induced acute liver failure, including 7 [5%] for herbal medications, none were specifically attributed to a product containing lemon balm).
- García-Cortés M, Borraz Y, Lucena MI, Peláez G, Salmerón J, Diago M, Martínez-Sierra MC, et al. [Liver injury induced by "natural remedies": an analysis of cases submitted to the Spanish Liver Toxicity Registry]. Rev Esp Enferm Dig 2008; 100: 688-95. Spanish. PubMed PMID: 19159172.
- (Among 521 cases of drug induced liver injury submitted to Spanish registry, 13 [2%] were due to herbals, but none were attributed to lemon balm).

- Navarro VJ. Herbal and dietary supplement hepatotoxicity. Semin Liver Dis 2009; 29: 373-82. PubMed PMID: 19826971.
- (Review of the problems of causality assessment in herbal and dietary supplement [HDS] associated liver disease, including the variable clinical presentations, the complexity and lack of information on their components, absence of controlled trials demonstrating safety and efficacy, the possibility of contamination or incorrect labeling, and the frequent underreporting of herbal use by patients. Regulation of HDS is under DSHEA, which requires manufacturers to determine safety and prohibits claims of efficacy in treating specific diseases. The US Pharmacopeia sets standards for food and drugs and includes HDS; HDS induced liver injury is a growing problem and currently accounts for at least 10% of cases of acute liver injury due to medications).
- Jacobsson I, Jönsson AK, Gerdén B, Hägg S. Spontaneously reported adverse reactions in association with complementary and alternative medicine substances in Sweden. Pharmacoepidemiol Drug Saf 2009; 18: 1039-47. PubMed PMID: 19650152.
- (Review of 778 spontaneous reports of adverse reactions to herbals to Swedish Registry; no mention of lemon balm).
- Reuben A, Koch DG, Lee WM; Acute Liver Failure Study Group. Drug-induced acute liver failure: results of a U.S. multicenter, prospective study. Hepatology 2010; 52: 2065-76. PubMed PMID: 20949552.
- (Among 1198 patients with acute liver failure enrolled in a US prospective study between 1998 and 2007, 133 [11%] were attributed to drug induced liver injury of which 12 [9%] were due to herbals, but none were attributed to lemon balm).
- Teschke R, Wolff A, Frenzel C, Schulze J, Eickhoff A. Herbal hepatotoxicity: a tabular compilation of reported cases. Liver Int 2012; 32: 1543-56. PubMed PMID: 22928722.
- (A systematic compilation of all publications on the hepatotoxicity of specific herbals identified 185 publications on 60 different herbs, herbal drugs and supplements, but lemon balm was not listed or mentioned).
- Navarro VJ, Barnhart H, Bonkovsky HL, Davern T, Fontana RJ, Grant L, Reddy KR, et al. Liver injury from herbals and dietary supplements in the U.S. Drug-Induced Liver Injury Network. Hepatology 2014; 60: 1399-408. PubMed PMID: 25043597.
- (Among 85 cases of HDS associated liver injury [not due to anabolic steroids] enrolled in a US prospective study between 2004 and 2013, none were attributed to a product containing lemon balm).
- Chalasani N, Bonkovsky HL, Fontana R, Lee W, Stolz A, Talwalkar J, Reddy KR, et al.; United States Drug Induced Liver Injury Network. Features and outcomes of 899 patients with drug-induced liver injury: The DILIN Prospective Study. Gastroenterology 2015; 148: 1340-52.e7. PubMed PMID: 25754159.
- (Among 899 cases of drug induced liver injury enrolled in a prospective database between 2004 and 2012, HDS were implicated in 145 [16%], the single major herbal cause being green tea, and none were attributed to lemon balm [see also Navarro et al Hepatology 2014]).
- García-Cortés M, Robles-Díaz M, Ortega-Alonso A, Medina-Caliz I, Andrade RJ. Hepatotoxicity by dietary supplements: A tabular listing and clinical characteristics. Int J Mol Sci 2016; 17: 537. PubMed PMID: 27070596.
- (Listing of published cases of liver injury from HDS products does not mention or list lemon balm).
- Brown AC. An overview of herb and dietary supplement efficacy, safety and government regulations in the United States with suggested improvements. Part 1 of 5 series. Food Chem Toxicol 2017; 107: 449-71. PubMed PMID: 27818322.
- (Summary of the US regulations on safety and efficacy of herbal and dietary supplements).
- Brown AC. Liver toxicity related to herbs and dietary supplements: Online table of case reports. Part 2 of 5 series. Food Chem Toxicol 2017; 107: 472-501. PubMed PMID: 27402097.

- (Description of an online compendium of cases of liver toxicity attributed to HDS products, does not mention or list lemon balm).
- Navarro VJ, Khan I, Björnsson E, Seeff LB, Serrano J, Hoofnagle JH. Liver injury from herbal and dietary supplements. Hepatology 2017; 65: 363-73. PubMed PMID: 27677775.
- (Review of the problems of liver injury and HDS products, mentions that multiingredient dietary supplements account for the major of cases, but does not mention a product with lemon balm as a component).
- Taavoni S, Nazem Ekbatani N, Haghani H. Valerian/lemon balm use for sleep disorders during menopause. Complement Ther Clin Pract. 2013;19:193-6. PubMed PMID: 24199972.
- (Among 58 postmenopausal women with decreased sexual desire treated with lemon balm [1 g] or placebo daily for 4 weeks, Pittsburgh Sleep Quality Index scores improved in both groups but more with lemon balm, and "no negative effects were observed"; no mention of ALT levels or hepatotoxicity).
- Jandaghi P, Noroozi M, Ardalani H, Alipour M. Lemon balm: A promising herbal therapy for patients with borderline hyperlipidemia a randomized double-blind placebo-controlled clinical trial. Complement Ther Med. 2016;26:136-40. PubMed PMID: 27261994.
- (Among 58 adults with hypercholesterolemia treated with lemon balm [3 g] or placebo daily for 12 weeks, minor side effects included occasional headache and dizziness, and total cholesterol levels did not change, although LDL cholesterol decreased in the lemon balm group [139 to 126 mg/dL] but not with placebo [130 to 131 mg/dL] and serum ALT and AST levels did not change with lemon balm treatment).
- Shakeri A, Sahebkar A, Javadi B. Melissa officinalis L. A review of its traditional uses, phytochemistry and pharmacology. J Ethnopharmacol. 2016;188:204-28. PubMed PMID: 27167460.
- (Review of the botanical characteristics, traditional uses, phytochemistry, pharmacological activities, pharmacokinetics, and toxicity of Melissa officinalis mentions that it is generally well tolerated and adverse events are no more frequent with lemon balm than placebo, uncommon adverse events may include dizziness, headache, nausea, abdominal pain, decreased appetite, and wheezing, but no serious adverse events have been reported and or significant changes in laboratory test results).
- Darvish-Mofrad-Kashani Z, Emaratkar E, Hashem-Dabaghian F, Emadi F, Raisi F, Aliasl J, Kamalinejad M, et al. Effect of Melissa officinalis (lemon balm) on sexual dysfunction in women: a double- blind, randomized, placebo-controlled study. Iran J Pharm Res. 2018;17(Suppl):89-100. PubMed PMID: 29796033.
- (Among 58 women with decreased sexual desire treated with lemon balm [1 g] or placebo daily for 4 weeks, those on lemon balm had improvements in sexual desire, arousal, lubrication, organism, and satisfaction with less pain during intercourse, and adverse events were mild and more frequent with placebo than lemon balm).
- Haybar H, Javid AZ, Haghighizadeh MH, Valizadeh E, Mohaghegh SM, Mohammadzadeh A. The effects of Melissa officinalis supplementation on depression, anxiety, stress, and sleep disorder in patients with chronic stable angina. Clin Nutr ESPEN. 2018;26:47-52. PubMed PMID: 29908682.
- (Among 73 patients with chronic, stable angina pectoris treated with lemon balm [3 g daily] or placebo, symptoms of depression, anxiety and stress decreased more with lemon balm; no mention of adverse events or ALT levels during therapy).
- Mirabi P, Alamolhoda SH, Yazdkhasti M, Mojab F. The effects of lemon balm on menstrual bleeding and the systemic manifestation of dysmenorrhea. Iran J Pharm Res. 2018;17(Suppl2):214-223. PubMed PMID: 31011354.
- (Among 90 students with dysmenorrhea treated with lemon balm [330 mg] or placebo three times daily for two menstrual cycles, symptoms of dysmenorrhea decreased in both groups to a similar degree; no mention of side effects or ALT levels during therapy).

- Watson K, Hatcher D, Good A. A randomised controlled trial of lavender (Lavandula angustifolia) and lemon balm (Melissa officinalis) essential oils for the treatment of agitated behaviour in older people with and without dementia. Complement Ther Med. 2019;42:366-373. PubMed PMID: 30670268.
- (Among 49 nursing home residents treated with lemon balm, lavender, or placebo once daily for 2 weeks in a double blind cross-over design, neither drug was associated with an improvement in behavior and lemon balm and lavender had discordant effects on agitation in those with and without dementia; no mention of adverse events, ALT levels, or liver toxicity).
- Ghazizadeh J, Sadigh-Eteghad S, Marx W, Fakhari A, Hamedeyazdan S, Torbati M, Taheri-Tarighi S, et al. The effects of lemon balm (Melissa officinalis L.) on depression and anxiety in clinical trials: A systematic review and meta-analysis. Phytother Res. 2021;35:6690-6705. PubMed PMID: 34449930.
- (Systematic review of the literature of randomized controlled trials of lemon balm in patients with anxiety or depression or both identified 6 adequately rigorous studies in 435 patients, the metaanalysis showing a slight quantitative effect of lemon balm on acute anxiety and both acute and chronic depression without serious side effects; no mention of ALT elevations or hepatotoxicity).