



## Centella asiatica

Updated: April 24, 2024.

## OVERVIEW

### Introduction

*Centella asiatica*, commonly known as gotu kola or Asian pennywort, is a herbaceous, flowering, perennial plant native to tropical areas of Southeast Asia and Australia and used as a food as well as in traditional medicine. While generally regarded as safe, *Centella* has been linked to rare instances of clinically apparent acute liver injury with jaundice.

### Background

*Centella* also known as gotu kola, tiger grass or Indian pennywort is made from fresh or dried leaves of *Centella asiatica* a creeping herbaceous, flowering plant native to tropical swampy areas of Southeast Asia and Australia but now found in many tropical and subtropical areas of the world. It is eaten as a vegetable and in salads and has been used for centuries in traditional Ayurvedic and Chinese medicine for a large variety of conditions. *Centella* extracts contain more than 100 constituents including polyacetylenes, flavonoids, flavones, sterols and lipids. The active ingredients are thought to be the pentacyclic triterpenoid glycosides, asiaticoside, centelloside, and madecassoside, and their aglycones, asiatic acid and madecassic acid. In vitro and in vivo studies suggest that these triterpenoids have anxiolytic, antiinflammatory, antioxidant, antiulcer, anticancer, neuroprotective, and wound healing properties. In traditional medicine, gotu kola has been used to treat a wide variety of conditions including minor wounds, psoriasis, cellulitis, chronic venous insufficiency, ulcers, hypertension, bronchitis, asthma, kidney disorders, urethritis, edema, diabetic microangiopathy, obesity, leprosy, smallpox, syphilis, and miscellaneous liver, kidney, pulmonary, and heart diseases. It is purported to promote immune function, to extend longevity, and to boost memory and cognitive function. However, none of these properties have been proven in prospective, controlled trials in humans, and *Centella asiatica* is not approved in the United States as therapy of any medical condition. Nevertheless, it is widely available as capsules, tablets, powders, solutions, and skin creams in over-the-counter herbal products. The typical oral dose is 60 to 120 mg daily of purified extracts, but may be 600 to 1800 mg daily of capsules or powders of dried leaves. *Centella* has few if any adverse events and no known proven severe adverse effects. In small trials, *Centella asiatica* extracts have appeared to be well tolerated with only mild, transient, and nonspecific adverse effects (headache, dizziness, bloating, diarrhea, nausea), which often have been similar in frequency among persons receiving placebo or alternative treatments. Rare instances of allergic reactions have been reported, particularly with topical therapy of skin diseases and wounds. Hepatotoxicity has also been reported but is very rare.

## Hepatotoxicity

Centella extracts have 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. Nevertheless, rare instances of acute and symptomatic liver injury have been published, including a case series in 2008 of three Argentinian women who developed liver injury with jaundice after use of centella for weight loss (Case 1) and a single short case report from Switzerland in 2011 after its oral use for acne. The time to onset ranged from 3 to 8 weeks and the injury was described as hepatocellular, resolving completely within 1 to 2 months after stopping. Immunoallergic and autoimmune features were present in some cases. The possibility of contamination or presence of other potential hepatotoxins in the commercial products was not ruled out in the clinical reports of hepatotoxicity of centella.

Likelihood score: C (probable rare cause of clinically apparent liver injury).

## Mechanism of liver injury

The mechanism of liver injury attributed to *Centella asiatica* is not known, but the rare events suggest idiosyncratic, perhaps immune mediated injury due to one of the many components of the herb or one of its metabolites.

## Outcome and Management

Gotu kola hepatotoxicity is generally self-limited and only mild-to-moderate in severity. Appearance of clinically evident liver injury developing during therapy should lead to prompt withdrawal of the herbal product. Rechallenge should be avoided.

## CASE REPORT

### Case 1. Acute granulomatous hepatitis developing during weight loss treatment with *Centella asiatica*. (1)

A 61 year old previously healthy woman developed abdominal pain, arthralgias, and weakness followed by dark urine and jaundice after taking tablets of *Centella asiatica* for 30 days as a weight loss agent. On examination she was jaundiced and had tender hepatomegaly. Laboratory tests (Table) showed marked elevations of serum ALT and AST (30 and 26 times the upper limit of normal [ULN]) with mild elevations in alkaline phosphatase (1.7 times ULN) and bilirubin (4.2 mg/dL). Viral serology showed no evidence of hepatitis A, B or C, while autoantibody testing showed high titers of SMA (1:160) and AMA (1:320) with no detectable ANA or anti-LKM, and normal total globulin levels. Liver ultrasound was normal. A liver biopsy showed an acute hepatitis with granulomas. She was treated with ursodiol and recovered. Two months later all laboratory results were normal or negative including SMA and AMA. She did well until 7 months later when she restarted *Centella asiatica* for two weeks when she developed pain, weakness and jaundice again. Laboratory results were similar to those with the first episode but ANA, SMA and AMA were still negative. A repeat liver biopsy again showed acute hepatitis with granulomatous changes. She was treated with a course of prednisone and ursodiol and again improved.

## Key Points

Medication:	<i>Centella asiatica</i>
Pattern:	Hepatocellular (R=17.6)
Severity:	3+ (jaundice, hospitalized)
Latency:	30 days initially, 14 days on re-exposure

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Recovery:	1-2 months
Other medications:	None mentioned

## Laboratory Values

Time After Starting	Time After Stopping	ALT (U/L)	Alk P (U/L)	Bilirubin (mg/dL)	Comments
1 month	0	1193	503	4.2	SMA 1:160, AMA 1:320
	< 1 week	Liver biopsy: acute hepatitis with granulomatous changes			
3 months	1 month	18	191	1.2	SMA & AMA negative
0	0	<b>Restarts Centella asiatica</b>			
2 weeks	0	413	383	2.8	ANA, SMA & AMA negative
	< 1 week	Liver biopsy: acute hepatitis with granulomatous changes			
1.5 months	1 month	27	238	0.6	Ursodiol & prednisone stopped
8 years	8 years	Laboratory values remained normal during follow up			
<b>Normal Values</b>		<b>&lt;40</b>	<b>&lt;301</b>	<b>&lt;1.2</b>	

## Comment

A dramatic case of an immunoallergic acute hepatitis arising in an otherwise healthy woman taking a commercial weight loss product said to be *Centella asiatica*. The clinical history, laboratory tests, liver biopsy, and recurrence on re-exposure provide convincing evidence of drug induced liver injury from the herbal product. At issue is whether the product consisted of *Centella asiatica* only. The history could also be consistent with other better known herbal causes of acute liver injury such as ephedra, chaparral, germander, garcinia, or green tea. The product name, concentration of centella, number of tablets taken daily, chemical analysis, and even product label were not provided. After these 3 cases from a single referral center in Mendoza, Argentina in 2005, there have been no published case series of injury from *Centella asiatica* and only a single case report from Switzerland in 2011. Furthermore, the large series of herbal and dietary supplement induced liver injury from around the world, there have been no further described cases.

Other Names: Gotu kola, Asian pennywort, spadeleaf, coinwort, tiger grass, Brahmi, Centella

Drug Class: [Herbal and Dietary Supplements](#)

## PRODUCT INFORMATION

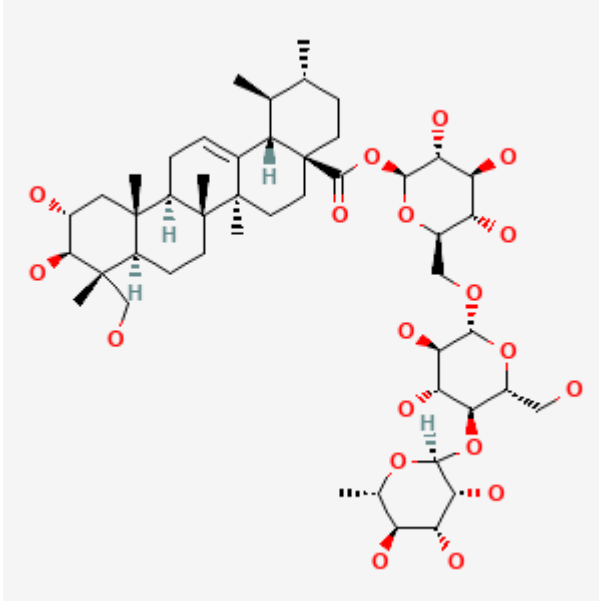
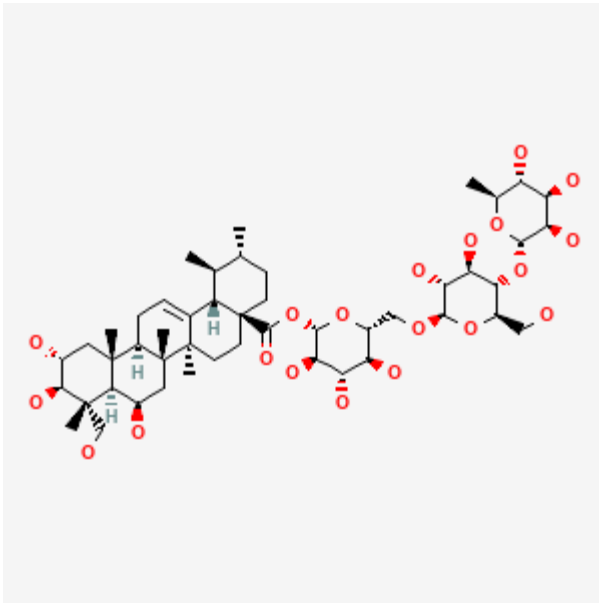
### REPRESENTATIVE TRADE NAMES

Centella asiatica – Generic

### DRUG CLASS

Herbal and Dietary Supplements

## CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NUMBER	MOLECULAR FORMULA	STRUCTURE
Asiaticoside	16830-15-2	C <sub>48</sub> H <sub>78</sub> O	
Madecassoside	34540-22-2	C <sub>48</sub> H <sub>78</sub> O <sub>20</sub>	

\* Major pentacyclic triterpenoid glycosides found in *Centella asiatica*.

## CITED REFERENCES

1. Jorge OA, Jorge AD. Hepatotoxicity associated with the ingestion of *Centella asiatica*. *Rev Esp Enferm Dig.* 2005;97:115-24. PubMed PMID: 15801887.

## SELECTED ANNOTATED BIBLIOGRAPHY

References updated: 24 April 2024

Abbreviation: 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 neither Centella asiatica or gotu kola are 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 gotu kola).*
- Gotu kola (*Centella asiatica*). PDR for Herbal Medicines. 4th ed. Montvale, New Jersey: Thomson Healthcare Inc. 2007: pp 400-404.
- (Compilation of short monographs on herbal medications and dietary supplements mentions allergic contact dermatitis and infertility but not ALT elevations or hepatotoxicity).*
- 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).*
- Bradwejn J, Zhou Y, Koszycki D, Shlik J. A double-blind, placebo-controlled study on the effects of Gotu Kola (*Centella asiatica*) on acoustic startle response in healthy subjects. *J Clin Psychopharmacol.* 2000;20:680-4. PubMed PMID: 11106141.
- (Among 40 healthy adult volunteers given a single 12 gram oral dose of gotu kola or placebo in grape juice, the acute startle response decreased more in those given the herb [-68% vs -29%], while pulse, blood pressure and mood ratings [anxiety, depression] did not change; no mention of hepatotoxicity and laboratory tests were not done).*
- 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 gotu kola).*
- Jorge OA, Jorge AD. Hepatotoxicity associated with the ingestion of *Centella asiatica*. *Rev Esp Enferm Dig.* 2005;97:115-24. PubMed PMID: 15801887.
- (3 Argentinian women developed jaundice 30, 20, and 60 days after starting Centella asiatica for weight loss [bilirubin 4.3, 19.9, and 3.9 mg/dL, ALT 1193, 1694, and 324 U/L, Alk P 503, 472, and 484 U/L], biopsies showing hepatitis with granulomas and zone 3 necrosis, high titers of autoantibodies found in one case [Case 1 above], all resolving completely with 1-2 months of stopping).*
- Chitturi S, Farrell GC. Hepatotoxic slimming aids and other herbal hepatotoxins. *J Gastroenterol Hepatol.* 2008;23:366-73. PubMed PMID: 18318821.
- (Review of liver injury from herbal agents taken for weight loss mentions the 3 cases due to Centella asiatica as reported by Jorge [2005]).*
- 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 gotu kola).*

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 gotu kola or Centella asiatica).*

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 gotu kola).*

Gohil KJ, Patel JA, Gajjar AK. Pharmacological Review on Centella asiatica: A potential herbal cure-all. *Indian J Pharm Sci.* 2010;72:546-56. PubMed PMID: 21694984.

*(Review of the botany and possible mechanisms of action of Centella asiatica extracts based upon laboratory studies in rodents and clinical trials in humans states that it “has no known toxicity in recommended doses” and that side effects are rare but may include skin allergy, headache, stomach upset, nausea, dizziness, and drowsiness particularly at high doses, and that it should not be used for more than 6 weeks).*

Dantuluri S, North-Lewis P, Karthik SV. Gotu Kola induced hepatotoxicity in a child - need for caution with alternative remedies. *Dig Liver Dis.* 2011;43:500. PubMed PMID: 21334992.

*(15 year old female developed abdominal pain 6 weeks after starting gotu kola for acne [bilirubin 1.8 mg/dL, ALT 319 rising to 3222 U/L, GGT 39 U/L, INR 2.7], improving rapidly upon stopping).*

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, mentions 3 cases attributed to gotu kola as reported by Jorge [2005]).*

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 Centella asiatica).*

Chalasanani 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 Centella asiatica or gotu kola [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. pii: 537. PubMed PMID: 27070596.

*(Listing of published cases of liver injury from HDS products does not mention or list gotu kola or Centella asiatica).*

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, mentions 4 cases attributed to gotu kola, 3 as reported by Jorge [2005] and 1 by Dantuluri [2011]).*

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 gotu kola as a component).*

Haslan H, Suhaimi FH, Das S. Herbal supplements and hepatotoxicity: a short review. *Nat Prod Commun.* 2015;10:1779-84. PubMed PMID: 26669124.

*(Review of liver injury due to herbal supplements mentions the 3 cases of jaundice caused by Centella asiatica as reported by Jorge [2005]).*

Santos G, Gasca J, Parana R, Nunes V, Schinnoni M, Medina-Caliz I, Cabello MR, Lucena MI, et al. Profile of herbal and dietary supplements induced liver injury in Latin America: A systematic review of published reports. *Phytother Res.* 2021;35:6-19. PubMed PMID: 32525269.

*(Review of reports of liver injury due to herbal supplements reported from Latin America lists the 3 cases of hepatitis attributed to Centella asiatica reported by Jorge from Argentina [2005]).*

Torbati FA, Ramezani M, Dehghan R, Amiri MS, Moghadam AT, Shakour N, Elyasi S, et al. Ethnobotany, phytochemistry and pharmacological features of Centella asiatica: a comprehensive review. *Adv Exp Med Biol.* 2021;1308:451-499. PubMed PMID: 33861456.

*(Review of the chemistry, possible mechanisms of action, and clinical uses of Centella asiatica; mentions the cases of hepatotoxicity published by Jorge [2005] but cites studies in rats showing no abnormalities in ALT or AST even with the highest doses used).*

Biswas D, Mandal S, Chatterjee Saha S, Tudu CK, Nandy S, Batiha GE, et al. Ethnobotany, phytochemistry, pharmacology, and toxicity of Centella asiatica (L.) Urban: A comprehensive review. *Phytother Res.* 2021;35:6624-6654. PubMed PMID: 34463404.

*(Review of the phytochemistry, pharmacology and toxicity of Centella asiatica mentions that it is cultivated in semi-aquatic environments and is used as a food as well as medicinal herb to treat minor wounds, eczema, ulcers, diarrhea, measles, jaundice, asthma, diabetes, toothache, smallpox, leprosy, syphilis, dementia, and digestive disorders, and that it is well tolerated in human subjects with no major undesirable effects, but also mentions the 3 cases of jaundice reported by Jorge [2005]).*

Bessone F, García-Cortés M, Medina-Caliz I, Hernandez N, Parana R, Mendizabal M, Schinoni MI, et al. Herbal and dietary supplements-induced liver injury in Latin America: experience from the LATINDILI Network. *Clin Gastroenterol Hepatol.* 2022;20:e548-e563. PubMed PMID: 33434654.

*(Among 367 cases of hepatotoxicity enrolled in the Latin American DILI Network between 2011 and 2019, 29 [8%] were attributed to herbal products, the most frequent being green tea [n=7], Herbalife products [n=5] and garcinia [n=3]; Centella asiatica and gotu kola are not mentioned).*

Ballotin VR, Bigarella LG, Brandão ABM, Balbinot RA, Balbinot SS, Soldara J. Herb-induced liver injury: Systematic review and meta-analysis. *World J Clin Cases.* 2021;9:5490-5513. PubMed PMID: 34307603.

*(Systematic review of the literature on herb induced liver injury identified 446 references describing 936 cases due to 79 different herbal products, the most common being He Shou Wu [91], green tea [90] Herbalife products [64], kava kava [62] and greater celandine [48]; Centella asiatica is listed as implicated in 3 cases as described by Jorge [2005]).*

Bandopadhyay S, Mandal S, Ghorai M, Jha NK, Kumar M, Ghosh A, et al. Therapeutic properties and pharmacological activities of asiaticoside and madecassoside: A review. *J Cell Mol Med.* 2023;27:593-608. PubMed PMID: 36756687.

*(Review of the phytochemistry and the biologic and clinical effects of asiaticoside and madecassoside, major triterpenoid glycosides of Centella asiatica, including neuroprotection, dermatologic healing, UV protection, pulmonary, renal, and liver protection, immunomodulatory, antiinflammatory, and antiallergic activities; no discussion of toxicity).*