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NLM Citation: LiverTox: Clinical and Research Information on Drug-Induced Liver Injury [Internet]. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases; 2012-. Greater Celandine. [Updated 2022 May 24].
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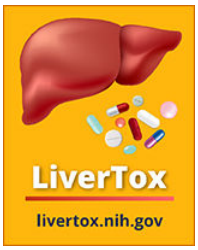

Greater Celandine

Updated: May 24, 2022.

OVERVIEW

Introduction

Greater celandine is a botanical extract derived from a plant of the Poppy family that is typically used for the treatment of gastrointestinal disorders and dyspepsia. Celandine has been linked to several instances of clinically apparent liver injury.

Background

Greater celandine (Chelidonium majus) is a plant of the Poppy family (Papaveraceae) which grows wild in Asia and Europe and has been introduced widely in the United States. Leaf extracts may contain up to 20 alkaloids, including benzophenanthridines, protoberberines and hydroxycinnamic acid derivatives. For centuries, celandine has been used to treat gastrointestinal complaints, dyspepsia and gallbladder disease. The chemical compound responsible for the antispasmodic activity of greater celandine is unknown. Celandine also acts as a mild sedative and it has been used to treat asthma, bronchitis and whooping cough. In recent years, greater celandine extracts have been used largely as therapy for dyspepsia and gallbladder disease, but it has also been claimed to be beneficial for skin conditions, asthma and bronchitis and as a weight loss agent. No human studies have been done that substantiate the benefits of celandine in these conditions or to define its safety, tolerability and adverse effects.

Lesser celandine (Ranunculus ficaria or Ficaria verna), also known as fig celandine, is a flowering plant native to Europe and Western Asia that is unrelated to greater celandine. Lesser celandine belongs to the buttercup family and has brightly colored yellow petals. The plant is poisonous to domesticated grazing animals and considered an undesirable weed. Extracts of lesser celandine are astringents that are used topically to treat hemorrhoids (hence its common name “pilewort”). It is rarely taken as an oral herbal product.

Hepatotoxicity

Over a dozen publications, largely from Europe, have described clinically apparent acute liver injury attributable to greater celandine (Chelidonium majus). Liver injury typically arises after 1 to 6 months, with jaundice and moderate to marked elevations in serum aminotransferase levels. The pattern of injury is usually hepatocellular and the clinical presentation and liver histology resemble acute viral hepatitis. Immunoallergic features are uncommon, but autoantibodies may be present in low to moderate levels in many cases. The clinical syndrome, however, rarely resembles autoimmune hepatitis and usually resolves rapidly once the botanical is discontinued and without need of corticosteroid therapy. There have been no reports of greater celandine hepatotoxicity from the United States or the Americas.

Likelihood Score: B (uncommon but likely cause of clinically apparent liver injury).

Mechanism of Injury

Greater celandine extracts have many components, but none of them has been shown to be specifically hepatotoxic. The rare cases of liver injury due to greater celandine have had idiosyncratic features.

Outcome and Management

Hepatotoxicity from greater celandine is rare; some cases have been severe, but fatal cases and acute liver failure leading to liver transplantation has not been described. Recurrence with reexposure has been documented in several cases and rechallenge should be avoided.

Drug Class: Herbal and Dietary Supplements

CASE REPORT

Case 1. Acute hepatitis due to greater celandine.(1)

A 42 year old woman developed fever, muscle aches, headaches, fatigue and abdominal discomfort 2 weeks after starting an oral herbal preparation containing greater celandine (Chelidonium majus) for a skin condition. The fever resolved in two weeks, but she continued to have generalized fatigue and then developed dark urine, light colored stools and jaundice. She sought medical care and the herbal preparation was discontinued. She had no history of liver disease, did not drink alcohol and denied risk factors for viral hepatitis. She was taking no other medications. On examination, she was jaundiced but had no signs of chronic liver disease. Laboratory results showed normal blood counts, but hyperbilirubinemia (~8.1 mg/dL) and marked elevations in serum ALT (~2900 U/L). Because of worsening jaundice, she was transferred to a referral hospital (Table). Tests for hepatitis A, B and C were negative as were autoantibodies. Immunoglobulin levels were normal. Liver ultrasound showed no evidence of biliary obstruction. A liver biopsy showed lymphocytic infiltrates and spotty necrosis with cell drop out in central areas with cholestasis. Thereafter, she improved symptomatically and in follow up her liver tests returned to the normal range.

Key Points

Medication:	Greater celandine (Chelidonium majus)
Pattern:	Hepatocellular (R=11.7, at week 9)
Severity:	3+ (jaundice, hospitalization)
Latency:	2 weeks to symptoms, 5 weeks to jaundice
Recovery:	8 weeks
Other medications:	None

Laboratory Values

Time After Starting	Time After Stopping	ALT (U/L)*	AST (U/L)*	Bilirubin (mg/dL)*	**Comments**
		Started celandine for skin disorder			
5 weeks	0	3200		8.2	Celandine stopped
8 weeks	3 weeks	2900		10.8	Hospital transfer
9 weeks	4 weeks	1490	265	11.7	

Table continued from previous page.

Time After Starting	Time After Stopping	ALT (U/L)*	AST (U/L)*	Bilirubin (mg/dL)*	**Comments**
10 weeks	5 weeks	700		7.0	Liver biopsy
13 weeks	8 weeks	29	115	1.3	
Normal Values		**<30**	**<120**	**<1.2**	

* Values estimated from Figure 2 (laboratory parameters are mislabeled).

Comment

The case history is typical of greater celandine hepatotoxicity. Other causes of acute liver injury were appropriately excluded. The onset of injury within 2 to 5 weeks of starting and resolution within 8 weeks of stopping the herbal product provides good evidence that the liver injury was caused by it. Rechallenge is not necessary for the diagnosis; other cases of celandine hepatotoxicity have demonstrated recurrence upon rechallenge. Greater celandine was used widely in Europe but rarely in the United States, so virtually all published cases are from Europe, including Germany, Spain, Italy, Belgium and the Netherlands.

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Greater Celandine – Generic

DRUG CLASS

Herbal and Dietary Supplements

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NUMBER	MOLECULAR FORMULA	STRUCTURE
Greater Celandine	84603-56-5	Herbal mixture	Not applicable

CITED REFERENCES

1. Crijns AP, de Smet PA, van den Heuvel M, Schot BW, Haagsma EB. Ned Tijdschr Geneeskd. 2002;146:124–8. [Acute hepatitis after use of a herbal preparation with greater celandine (Chelidonium majus)]. Dutch. PubMed PMID: 11826672.

ANNOTATED BIBLIOGRAPHY

References updated: 24 May 2022

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; hepatotoxicity of herbals is discussed but not greater celandine specifically).

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 herbal and dietary supplements [HDS] mentions that greater celandine has been used in Europe to treat dyspepsia and gallstones and that multiple cases of acute hepatitis including a case series of 10 instances attributable to celandine have been published).

Celandine (*Chelidonium majus*). In, PDR for Herbal Medicines. 4th ed. Montvale, New Jersey: Thomson Healthcare Inc. 2007: pp. 180-1.

(Compilation of short monographs on herbal medications and dietary supplements).

Pinto García V, Vicente PR, Barez A, Soto I, Candas MA, Coma A. Sangre(Barc). 1990;35:401–3. [Hemolytic anemia induced by Chelidonium majus. Clinical case]. Spanish. PubMed PMID: 2291149.

(72 year old woman developed hemolytic anemia and renal dysfunction with hepatic involvement after taking greater celandine [bilirubin 1.7 mg/dL, ALT 538 U/L], resolving rapidly upon stopping).

De Smet PA, Van den Eertwegh AJ, Lesterhuis W, Stricker BH. Hepatotoxicity associated with herbal tablets. BMJ. 1996;313:92. PubMed PMID: 8688761.

(69 year old woman developed jaundice six weeks after starting herbal tablets "Venencapsan" prepared locally from horse chestnut leaf, milfoil, celandine, sweet clover, milk thistle and dandelion root, recurring on reexposure [bilirubin 1.6 and 4.7 mg/dL, ALT 244 and 1004 U/L, Alk P 229 and 250 U/L], and resolving rapidly on stopping).

Strahl S, Ehret V, Dahm HH, Maier KP. Dtsch Med Wochenschr. 1998;123:1410–4. [Necrotizing hepatitis after taking herbal remedies]. German. PubMed PMID: 9856112.

(42 year old woman developed repeated bouts of jaundice 6 months and then 6 weeks after staring celandine [bilirubin 3.6 and 4.4 mg/dL, ALT 427 and 389 U/L, GGT 87 U/L, Alk P 221 U/L], resolving within 2 months of stopping each time).

Greving I, Meister V, Monnerjahn C, Müller KM, May B. Chelidonium majus: a rare reason for severe hepatotoxic reaction. Pharmacoepidemiol Drug Saf. 1998;7 Suppl 1:S66–9. PubMed PMID: 15073964.

(Two cases: a 28 year old woman developed jaundice and itching 5 months after starting greater celandine [bilirubin 16.4 mg/dL, ALT 432 U/L], resolving in 2 months; 35 year old woman developed jaundice and abdominal pain 4 months after starting celandine [bilirubin 16.1 mg/dL, ALT 654 U/L], resolving within a few months of stopping).

Benninger J, Schneider HT, Schuppan D, Kirchner T, Hahn EG. Acute hepatitis induced by greater celandine (Chelidonium majus). Gastroenterology. 1999;117:1234–7. PubMed PMID: 10535888.

(Report of 10 cases of hepatitis attributed to greater celandine; all women, ages 37 to 67 years, taking celandine for digestive disorders or eczema for 1-9 months, presented with symptoms [bilirubin normal in 5 and 4.5-21.7 mg/dL in the rest, ALT 123-1338 U/L, Alk P 65-451 U/L], resolving within 2-6 months in all; one patient had recurrence on restarting celandine).

Chitturi S, Farrell GC. Drug-induced cholestasis. Semin Gastrointest Dis. 2001;12:113–24. PubMed PMID: 11352118.

(Review of hepatotoxicity manifested by prominent cholestatic features; discusses greater celandine, although usual presentation is with an acute hepatitis-like syndrome).

Stickel F, Seitz HK, Hahn EG, Schuppan D. Z Gastroenterol. 2001;39:225–32, 234-7. [Liver toxicity of drugs of plant origin]. German. PubMed PMID: 11324140.

(Review of hepatotoxicity of botanicals including pyrrolizidine alkaloids, germander, greater celandine, chaparral, Chinese herbs and pennyroyal).

De Smet PA. Safety concerns about kava not unique. Lancet. 2002;360(9342):1336. PubMed PMID: 12414243.

(Letter indicating that greater celandine like kava has been linked to several cases of severe liver injury and a warning label was added in Germany).

Crijns AP, de Smet PA, van den Heuvel M, Schot BW, Haagsma EB. Ned Tijdschr Geneeskd. 2002;146:124–8. [Acute hepatitis after use of a herbal preparation with greater celandine (Chelidonium majus)]. Dutch. PubMed PMID: 11826672.

(42 year old woman developed fever and abdominal pain 2 weeks after starting greater celandine, followed by fatigue and jaundice at 5 weeks [bilirubin 8.1 rising to 11.7 mg/dL, ALT 2900 U/L, Alk P 265 U/L], worsening for a few weeks and then resolving 2 months after stopping: Case 1).

van Noordwijk J. Ned Tijdschr Geneeskd. 2002;146:100–2. ["Dosis solum facit venenum" also for herbal products]. Dutch. PubMed PMID: 11826667.

(Editorial in response to Crijns [2002] "Search first for a poison, or for a plant product"; plant products are not necessarily safer than prescription medications).

Stedman C. Herbal hepatotoxicity. Semin Liver Dis. 2002;22:195–206. PubMed PMID: 12016550.

(Review and description of patterns of liver injury due to herbal medications, including discussion of potential risk factors, and herb-drug interactions; greater celandine has been implicated in 10 cases of acute hepatitis with onset within 3 months in most and resolution in all, generally within 2 to 6 months of stopping).

Stickel F, Pöschl G, Seitz HK, Waldherr R, Hahn EG, Schuppan D. Acute hepatitis induced by Greater Celandine (Chelidonium majus). Scand J Gastroenterol. 2003;38:565–8. PubMed PMID: 12795472.

(2 cases: 39 year old woman developed jaundice 4 weeks after starting celandine [bilirubin 7.1 rising to 13.5 mg/dL, ALT 912 U/L, Alk P 116 U/L], with recurrence on restarting and resolution in 7 weeks on stopping; 69 year old man developed jaundice 6 weeks after starting celandine [bilirubin 9.1 mg/dL, ALT 881 U/L, Alk P 312 U/L], with resolution on stopping).

Schiano TD. Hepatotoxicity and complementary and alternative medicines. Clin Liver Dis. 2003;7:453–73. PubMed PMID: 12879994.

(Comprehensive review of herbal associated hepatotoxicity, including common patterns of presentation and a specific discussion of greater celandine).

Pittler MH, Ernest E. Systematic review: hepatotoxic events associated with herbal medicinal products. Aliment Pharmacol Ther. 2003;18:451–71. PubMed PMID: 12950418.

(Systematic review of published cases of hepatotoxicity due to herbal medications listing 52 case reports or case series, most common agents being greater celandine [3], chaparral [3], germander [8], Jin Bu Huan [3], kava [1], Ma Huang [3], pennyroyal oil [1], skullcap [2], Chinese herbs [9], valerian [1]).

Estes JD, Stolpman D, Olyaei A, Corless CL, Ham JM, Schwartz JM, Orloff SL. High prevalence of potentially hepatotoxic herbal supplement use in patients with fulminant hepatic failure. Arch Surg. 2003;138:852–8. PubMed PMID: 12912743.

(Among 20 patients undergoing liver transplantation for acute liver failure during 2001-2, 10 were potentially caused by herbals: none were attributed to celandine).

Pak E, Esrason KT, Wu VH. Hepatotoxicity of herbal remedies: an emerging dilemma. Prog Transplant. 2004;14:91–6. PubMed PMID: 15264453.

(Review of hepatotoxicity of herbal medications stressing the recent rise in numbers of cases, with literature review of cases due to greater celandine).

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, but celandine not mentioned as a cause).

Rifai K, Flemming P, Manns MP, Trautwein C. Internist (Berl). 2006;47:749–51. [Severe drug hepatitis caused by Chelidonium]. German. PubMed PMID: 16645871.

(58 year old man developed jaundice and pruritus 3 weeks after starting greater celandine [bilirubin 9.6 mg/dL, ALT 903 U/L], resolving within 4 weeks of stopping).

Seeff LB. Herbal hepatotoxicity. Clin Liver Dis. 2007;11:577–96. PubMed PMID: 17723921.

(Review of herbal induced hepatotoxicity, with a review of the 13 cases of acute liver injury attributed to greater celandine in the literature).

Hardeman E, Van Overbeke L, Ilegems S, Ferrante M. Acute hepatitis induced by greater celandine (Chelidonium majus). Acta Gastroenterol Belg. 2008;71:281–2. PubMed PMID: 18720945.

(58 year old woman developed jaundice 3 weeks after starting greater celandine [bilirubin 19.9 rising to 27 mg/dL, ALT 1566 U/L, Alk P 316 U/L], resolving rapidly upon stopping; enlarged lymph nodes in porta hepatis and ascites; biopsy showing reactive change, resolving with stopping celandine).

Conti E, De Checchi G, Mencarelli R, Pinato S, Rovere P. Lycopodium similiaplex-induced acute hepatitis: a case report. Eur J Gastroenterol Hepatol. 2008;20:469–71. PubMed PMID: 18403950.

(46 year old woman developed nausea and fatigue 8 weeks after starting L similiaplex solution [L serratum and Chelidonium majus] for insomnia [bilirubin 3.2 mg/dL, ALT 2364 U/L, Alk P 255 U/L], with resolution in 2 months of stopping).

García-Cortés M, Borraz Y, Lucena MI, Peláez G, Salmerón J, Diago M, Martínez-Sierra MC, et al. Rev Esp Enferm Dig. 2008;100:688–95. [Liver injury induced by "natural remedies": an analysis of cases submitted to the Spanish Liver Toxicity Registry]. 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 greater celandine).

Chalasani N, Fontana RJ, Bonkovsky HL, Watkins PB, Davern T, Serrano J, Yang H, Rochon J; Drug Induced Liver Injury Network (DILIN). Causes, clinical features, and outcomes from a prospective study of drug-induced liver injury in the United States. Gastroenterology. 2008;135:1924–34. PubMed PMID: 18955056.

(Among 300 cases of drug induced liver disease in the US collected between 2004 and 2008, 9% of cases were attributed to herbal medications, but none were attributed to greater celandine).

Tarantino G, Pezzullo MG, Dario di Minno MN, Milone F, Pezzullo LS, Milone M, Capone D. Drug-induced liver injury due to "natural products" used for weight loss: a case report. World J Gastroenterol. 2009;15:2414–7. PubMed PMID: 19452589.

(22 year old woman developed jaundice, pruritus, fever and abdominal pain [bilirubin 7.5 g/dL, ALT 1686 U/L, Alk P 1229 U/L, eosinophils 7%], responding only partially to cholecystectomy and extraction of stones from the common bile duct, whereupon she was found to have been taking greater celandine and Lycopodium serratum).

Moro PA, Cassetti F, Giugliano G, Falce MT, Mazzanti G, Menniti-Ippolito F, Raschetti R, Santuccio C. Hepatitis from Greater celandine(Chelidonium majus L.): review of literature and report of a new case. J Ethnopharmacol. 2009;124:328–32. PubMed PMID: 19397968.

(Case report and review of 16 cases in the literature; 65 year old man developed jaundice one month after starting daily ingestion of tea made from greater celandine extract [Chelidonium majus] [bilirubin 6.4 mg/dL, ALT 4765 U/L], with resolution within 2 months of stopping).

Navarro VJ. Herbal and dietary supplement hepatotoxicity. Semin Liver Dis. 2009;29:373–82. PubMed PMID: 19826971.

(Overview of the regulatory environment, clinical patterns, and future directions in research with HDS; greater celandine is not discussed).

Teschke R, Glass X, Schulze J. Herbal hepatotoxicity by Greater Celandine (Chelidonium majus): causality assessment of 22 spontaneous reports. Regul Toxicol Pharmacol. 2011;61:282–91. PubMed PMID: 21893153.

(Analysis of 22 cases of liver injury attributed to greater celandine reported to the German Registry using RUCAM found only 8 to be probable: 3 men and 5 women, ages 32 to 66 years, with onset after 28 to 42 [mean = 36] days [bilirubin elevated in 7, ALT 420-2928 U/L, Alk P 256-408 U/L], all recovered).

Teschke R, Frenzel C, Glass X, Schulze J, Eickhoff A. Greater Celandine hepatotoxicity: a clinical review. Ann Hepatol. 2012;11:838–48. PubMed PMID: 23109446.

(Analysis of clinical features of 16 cases of hepatotoxicity attributed to greater celandine from the European literature; 6 men and 10 women, ages 32 to 69 years, onset after 3 weeks to 4.5 months, usually with a hepatocellular pattern of injury and resolving with stopping in all).

Teschke R, Glass X, Schulze J, Eickhoff A. Suspected Greater Celandine hepatotoxicity: liver-specific causality evaluation of published case reports from Europe. Eur J Gastroenterol Hepatol. 2012;24:270–80. PubMed PMID: 22189691.

(Among 21 published case reports of liver injury attributed to celandine, only 8 were scored as probable by the RUCAM system: 3 men and 5 women, ages 37 to 68 years, onset in 3-12 weeks [ALT 152-4765 U/L, Alk P 221-516 U/L], resolving in 1 to 5 months of 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 including 15 publications on greater celandine).

Bunchorntavakul C, Reddy KR. Review article: herbal and dietary supplement hepatotoxicity. Aliment Pharmacol Ther. 2013;37:3–17. PubMed PMID: 23121117.

(Systematic review of literature on HDS associated liver injury discusses the clinically apparent hepatotoxicity attributed to greater celandine, reported largely from Europe).

Teschke R, Schulze J, Schwarzenboeck A, Eickhoff A, Frenzel C. Herbal hepatotoxicity: suspected cases assessed for alternative causes. Eur J Gastroenterol Hepatol. 2013;25:1093–8. PubMed PMID: 23510966.

(Review of the literature of case series of suspected HDS related liver injury found evidence of other explanations for the liver injury in 19 of 23 publications involving 278 of 573 patients [49%], including 28 of 66 cases [42%] attributed to greater celandine, and that these other diagnoses weakened the causality assessment in most instances).

Teschke R, Genthner A, Wolff A, Frenzel C, Schulze J, Eickhoff A. Herbal hepatotoxicity: Analysis of cases with initially reported positive re-exposure tests. Dig Liver Dis. 2014;46:264–9. PubMed PMID: 24315480.

(Reanalysis of 34 published cases of liver injury due to herbal medications in which there was a reported positive rechallenge, finding only 21 [62%] fulfilled the criteria of a positive rechallenge using RUCAM, the others having inconsistent [18%] or incomplete data [21%]; among 3 cases attributed to greater celandine, 1 rechallenge was considered negative and 1 uninterpretable).

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;148:1340–1352.e7. PubMed PMID: 25754159.

(Among 899 cases of drug induced liver injury enrolled in a US prospective study between 2004 and 2013, 145 [16%] were attributed to herbal and dietary supplements, but none to greater celandine).

Yilmaz B, Yilmaz B, Aktaş B, Unlu O, Roach EC. Lesser celandine (pilewort) induced acute toxic liver injury: The first case report worldwide. World J Hepatol. 2015;7:285–8. PubMed PMID: 25729484.

(36 year old woman developed jaundice 10 days after starting drinking tea made from lesser [not greater] celandine also known as Ranunculus ficaria or "pilewort" [bilirubin 3.4 mg/dL, ALT 1830 U/L, Alk P 225 U/L], with rapid recovery upon stopping).

Frenzel C, Teschke R. Herbal hepatotoxicity: clinical characteristics and listing compilation. Int J Mol Sci. 2016;17:E588. pii. PubMed PMID: 27128912.

(Review of the challenges in the diagnosis of hepatotoxicity due to herbal products including problems of misidentifications, adulterants, impurities, range of clinical presentations, lack of diagnostic markers, and alternative diagnoses; an extensive compilation of herbs reported to have caused liver injury including greater celandine).

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, lists at least 6 publications of case reports and case series implicating greater celandine in causing liver injury).

Pantano F, Mannocchi G, Marinelli E, Gentili S, Graziano S, Busardò FP, di Luca NM. Hepatotoxicity induced by greater celandine (Chelidonium majus L.): a review of the literature. Eur Rev Med Pharmacol Sci. 2017;21(1 Suppl):46–52. PubMed PMID: 28379595.

(Review of the published literature on liver injury from greater celandine).

Medina-Caliz I, Garcia-Cortes M, Gonzalez-Jimenez A, Cabello MR, Robles-Diaz M, Sanabria-Cabrera J, Sanjuan-Jimenez R, et al; Spanish DILI Registry. Herbal and dietary supplement-induced liver injuries in the Spanish DILI Registry. Clin Gastroenterol Hepatol. 2018;16:1495–1502. PubMed PMID: 29307848.

(Among 856 cases of hepatotoxicity enrolled in the Spanish DILI Registry between 1994 and 2016, 32 were attributed to herbal products, the most frequent cause being green tea [n=8] and Herbalife products [n=6], only one of which was attributed to greater celandine, a 37 year old man with hepatocellular injury that resulted in liver transplantation in 2012).

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], while none were attributed to greater celandine).

Ballotin VR, Bigarella LG, Brandão ABM, Balbinot RA, Balbinot SS, Soldera 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 [n=91], green tea [90] Herbalife products [64], kava [62] and greater celandine [48]).