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Skullcap

Updated: March 28, 2020.

OVERVIEW

Introduction

Skullcap is Native American plant, the dried leaves and stems of which are used as an herbal medication and in teas to treat anxiety, stress and insomnia. Skullcap has been linked to several instances of clinically apparent liver injury, but usually in combination with other botanicals.

Background

Skullcap is a flowering perennial plant native to North America (Scutellaria lateriflora) used for centuries by Native Americans to treat menstrual disorders, nervousness, digestive and kidney problems. The name skullcap refers to the flower's resemblance to helmets worn by European soldiers. Skullcap was used formerly for nervous disorders, including hysteria, nervous tension, epilepsy and chorea. It is now used largely as a sedative and sleeping pill, often in combination with other herbs such as valerian. Skullcap extracts are prepared from the aerial parts of the Scutellaria lateriflora plant and contain large amounts of flavonoids, including scutellarin and baicalin, which are believed to be the active components accounting for its sedative and antispasmodic activity. It is thought that the flavonoid compounds may act as gamma amino butyric acid (GABA) agonists similar to the benzodiazepines. There are more than 200 species of Scutellaria which have different components and activities as well as potential toxicities. Skullcap is available as a powder to prepare in tea, as a liquid solution and in capsules. Scutellaria is listed as a component in many commercially available, over-the-counter herbal mixtures.

Hepatotoxicity

Skullcap has been implicated in rare instances of clinically apparent liver injury, although in most cases multiple herbal medications were being taken and the role of skullcap in the hepatic damage was unclear. Furthermore, in some instances phytochemical analysis has identified significant adulterants (germander) or mislabeling in cases of suspected skullcap hepatotoxicity. In reported cases, the onset of symptoms and jaundice occurred within 1 to 12 weeks of starting skullcap, and the serum enzyme pattern was typically hepatocellular. Immunoallergic and autoimmune features were usually absent, although low titers of autoantibodies were not infrequent. Recovery was rapid once the herbal was discontinued, but some cases have resulted in acute liver failure. Chinese skullcap is a different species, but may also have adverse effects on the liver. There have been several reports and small case series of acute liver injury with jaundice arising after 1 to 3 months of starting herbals or dietary supplements with Chinese skullcap (Scutellaria baicalensis), the liver injury resembling that associated with North American skullcap (Scutellaria lateriflora).

Likelihood score: B (very likely but rare cause of clinically apparent liver injury).

Mechanism of Injury

The mechanism of skullcap hepatotoxicity is not known.

Outcome and Management

Hepatotoxicity from skullcap is rare, and is usually mild-to-moderate in severity and resolves rapidly once the botanical is stopped. At least one case of acute liver failure has been reported with skullcap, but there have been no instances of chronic liver disease, cirrhosis or vanishing bile duct syndrome linked to skullcap administration.

Other Names: Blue pimpernel, Helmet flower, Hoodwort, Mad weed, Quaker bonnet, Scullcap, Scutellaria

Drug Class: Herbal and Dietary Supplements

CASE REPORT

Case 1. Acute hepatitis due to combination of skullcap and valerian.(1)

A 53 year old woman developed worsening insomnia, anxiety and jaundice 4 weeks after starting an herbal preparation for sleep that contained skullcap (Scutellaria lateriflora) and valerian root (Valeriana officianalis) for sleep. She had no history of liver disease, alcohol abuse or risk factors for viral hepatitis. She took no other medications except for a cup of herbal tea 2 to 3 times weekly which contained chaparral leaf (Larrea tridentate), and rare use of other miscellaneous herbals. On examination, she was jaundiced but had no fever, rash or signs of chronic liver disease. Laboratory testing showed a serum bilirubin of 9.0 mg/dL with marked increases in serum aminotransferase levels (ALT 1208 U/L, AST 1082 U/L), and modest increase in alkaline phosphatase (298 U/L) and normal prothrombin time and serum albumin (Table). The white count and differential were normal. Tests for hepatitis A, B and C were negative as were autoantibodies. Immunoglobulin levels revealed a slight increase in IgG (2240 mg/dL), but normal IgA and IgM. An anti-CMV IgM assay was positive, but urine cultures were negative and serial titers of anti-CMV were stable. Abdominal ultrasound showed no evidence of gallstones or biliary obstruction. A liver biopsy was not done. She was monitored on no therapy and improved steadily. One month later, the jaundice had resolved and 3 months after stopping the herbal, all liver tests were normal.

Key Points

Medication:	Skullcap and valerian (4 capsules nightly)
Pattern:	Hepatocellular (R=8.5)
Severity:	3+ (jaundice, hospitalization)
Latency:	4 weeks
Recovery:	12 weeks
Other medications:	None, except occasional herbal tea containing chaparral leaf

Laboratory Values

Time After Starting	Time After Stopping	ALT (U/L)	Alk P (U/L)	Bilirubin (mg/dL)	Comments
		Started sleeping aid with skullcap and valerian root			
4 weeks	0	1208	298	9.0	Admission, herbals stopped
8 weeks	4 weeks	161		Normal	

Table continued from previous page.

Time After Starting	Time After Stopping	ALT (U/L)	Alk P (U/L)	Bilirubin (mg/dL)	Comments
16 weeks	12 weeks	Normal	Normal	Normal	
Normal Values		**<65**	**<136**	**<1.2**	

Comment

The case history is entirely compatible with drug induced liver injury caused by one of the several botanicals that she was taking. Skullcap (Scutellaria lateriflora) has been associated with cases of clinically apparent liver injury, but largely in association with other botanicals that have also been implicated in causing hepatotoxicity. Valerian has been reported to cause an acute hepatitis-like syndrome alone or in combination with skullcap, both of which have purported sedative qualities leading to their mixture in herbal preparations claimed to help sleep.

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Skullcap – Generic

DRUG CLASS

Herbal and Dietary Supplements

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NUMBER	MOLECULAR FORMULA	STRUCTURE
Skullcap	94279-99-9	Herbal mixture	Not applicable

CITED REFERENCE

1. Caldwell SH, Feeley JW, Wieboldt TF, Featherston PL, Dickson RC. Acute hepatitis with use of over-the-counter herbal remedies. Va Med Q. 1994 Winter;121(1):31–3. PubMed PMID: 8142493.

ANNOTATED BIBLIOGRAPHY

References updated: 28 March 2020

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 skullcap is not specifically 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 herbal and dietary supplements [HDS]).

Scullcap. In, PDR for Herbal Medicines. 4th ed. Montvale, New Jersey: Thomson Healthcare Inc. 2007: pp. 739.

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

Harvey J, Colin-Jones DG. Mistletoe hepatitis. Br Med J(Clin Res Ed). 1981;282:186–7. PubMed PMID: 6779941.

(49 year old woman developed fatigue and abdominal pain on two occasions after a few weeks of taking an herbal containing mistletoe and skullcap [bilirubin 2.5 mg/dL, ALT >250 U/L, Alk P 123 U/L], resolving in 6-24 weeks, the authors attributed the injury to mistletoe).

Mizoguchi Y, Miyajima K, Sakagami Y, Yamamoto S. Nippon Naika Gakkai Zasshi. 1986;75:1453–6. [A severe case of drug-induced allergic hepatitis in herbal medicine]. Japanese. PubMed PMID: 3805846.

(A 27 year old developed jaundice 6 weeks after taking Kinshigan, a Kampo herb with rapid recovery, but recurring with a more severe course 2 weeks after restarting [bilirubin 28.5 mg/dL, ALT 166 U/L, Alk P 1.5 times ULN, 1% eosinophils]; among 18 ingredients of the product was Scuttelariae radix).

MacGregor FB, Abernethy VE, Dahabra S, Cobden I, Hayes PC. Hepatotoxicity of herbal remedies. BMJ. 1989;299:1156–7. PubMed PMID: 2513032.

(Four cases of hepatitis attributed to herbals, all women, ages 41-57, developed jaundice 2 to 8 weeks after starting herbals for stress ["Neurelax" and "Kalms"] believed to contain skullcap and/or valerian [bilirubin 13.5-28.3 mg/dL, ALT 293-1165 U/L, Alk P 97-730 U/L], resolving 2-19 months after stopping).

Miskelly FG, Goodyer LI. Hepatic and pulmonary complications of herbal medicines. Postgrad Med J. 1992;68:935. PubMed PMID: 1494520.

(77 year old woman developed fatigue followed by jaundice 6 months after starting an herbal product with comfrey and skullcap [bilirubin 3.5 mg/dL, AST 520 U/L, Alk P 390 U/L], resolving within 6 months of stopping).

Bruseth S, Enge A. Tidsskr Nor Laegeforen. 1992;112:2389–90. [Scullcap—liver damage. Mistletoe hepatitis]. Norwegian. PubMed PMID: 1369618.

(Letter mentioning that mistletoe has been implicated in causing liver injury, but that the patient was also taking skullcap; mistletoe has been used in more than 30,000 cancer patients with no evidence of liver injury, although allergic reactions have been reported).

Caldwell SH, Feeley JW, Wieboldt TF, Featherston PL, Dickson RC. Acute hepatitis with use of over-the-counter herbal remedies. Va Med Q. 1994;121:31–3. PubMed PMID: 8142493.

(53 year old woman developed jaundice 4 weeks after starting an herbal for sleep containing skullcap and valerian given as 4 capsules nightly [bilirubin 9 mg/dL, ALT 1208 U/L, Alk P 298 U/L, protime 13.5 sec], resolving within 3 months of stopping: Case 1).

Hullar TE, Sapers BL, Ridker PM, Jenkins RL, Huth TS, Farraye FA. Herbal toxicity and fatal hepatic failure. Am J Med. 1999;106:267–8. PubMed PMID: 10230761.

(28 year old man developed jaundice after taking skullcap and pau d'arco for 6 months for his multiple sclerosis [bilirubin 29.0 mg/dL, ALT 3917 U/L, Alk P 106 U/L, protime 20 seconds, ANA 1:640], progressing to liver failure and liver transplant 5 weeks later, dying shortly thereafter; explant showed sinusoidal obstruction 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, celandine, chaparral, Chinese herbs and pennyroyal).

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

(Review and description of patterns of liver injury, including discussion of potential risk factors, and herb-drug interactions; skullcap is listed as potentially causing veno-occlusive disease).

Whiting PW, Clouston A, Kerlin P. Black cohosh and other herbal remedies associated with acute hepatitis. Med J Aust. 2002;177:440–3. PubMed PMID: 12381254.

(6 cases of severe hepatitis in patients taking herbal medications, including one on black cohosh alone and 5 taking multiple herbals including skullcap [n=3], valerian [n=2], chaparral [n=1] and greater celandine [n=1] for 1-14 weeks, presenting with jaundice [bilirubin 9.9-62.7 mg/dL, ALT 1293-3764 U/L, Alk P 80-219 U/L], 1 on black cohosh alone requiring liver transplantation, the other 5 resolving in 7-25 weeks; 3 were treated with prednisone for prolonged cholestasis).

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; mentions two reports of hepatotoxicity due to skullcap).

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 celandine [3], chaparral [3], germander [8], Jin Bu Huan [3], kava [1], Ma Huang [3], pennyroyal [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: 3 Ma Huang, 3 kava, 2 LipoKinetix, 1 chaparral, 1 skullcap and 2 miscellaneous Chinese herbs).

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 skullcap not mentioned as a cause).

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

(Review of herbal induced hepatotoxicity, with a review of two reports of acute liver injury attributed to skullcap in the literature).

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 skullcap).

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, skullcap is not listed).

Lin LZ, Harnly JM, Upton R. Comparison of the phenolic component profiles of skullcap (Scutellaria lateriflora) and germander (Teucrium canadense and T. chamaedrys), a potentially hepatotoxic adulterant. Phytochem Anal. 2009;20:298–306. PubMed PMID: 19402188.

(Herbal extracts of skullcap [S. lateriflora]) have occasionally been contaminated with germander [T. chamaedrys], but mass spectrometry can separate the two by demonstration of phenylethanoid components of germander).

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; skullcap is not discussed).

Morgan SL, Baggott JE, Moreland L, Desmond R, Kendrach AC. The safety of flavocoxid, a medical food, in the dietary management of knee osteoarthritis. J Med Food. 2009;12:1143–8. PubMed PMID: 19857081.

(Among 59 patients with osteoarthritis treated with flavocoxid [a medical food that contains baicalin extracted from Scutellaria baicalensis] vs placebo for 12 weeks, side effects were minor, and mean ALT or AST values did not change).

Levy R, Khokhlov A, Kopenkin S, Bart B, Ermolova T, Kantemirova R, Mazurov V, Bell M, Caldron P, Pillai L, Burnett B. Efficacy and safety of flavocoxid compared with naproxen in subjects with osteoarthritis of the knee- a subset analysis. Adv Ther. 2010;27:953–62. PubMed PMID: 20972845.

(Among 220 patients with osteoarthritis treated with flavocoxid [a medical food that contains baicalin] or naproxen for 12 weeks, rates of ALT elevations were similar and none were >5 times ULN or associated with symptoms or jaundice).

Pillai L, Burnett BP, Levy RM; GOAL Study Cooperative Group. GOAL: multicenter, open-label, post-marketing study of flavocoxid, a novel dual pathway inhibitor anti-inflammatory agent of botanical origin. Curr Med Res Opin. 2010;26:1055–63. PubMed PMID: 20225990.

(Among 1005 patients with osteoarthritis treated with flavocoxid [a medical food that contains baicalin] in an open label study, only one subject had liver test abnormalities, but no details given).

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 skullcap).

Linnebur SA, Rapacchietta OC, Vejar M. Hepatotoxicity associated with Chinese skullcap contained in Move Free Advanced dietary supplement: two case reports and review of the literature. Pharmacotherapy 2010; 3(7): 750, 258e-262e.

(Two patients developed liver injury within weeks of taking "Move Free Advanced", which contains Chinese skullcap [Scutellaria baicalensis] for arthralgias, resolving upon stopping).

Stickel F, Kessebohm K, Weimann R, Seitz HK. Review of liver injury associated with dietary supplements. Liver Int. 2011;31:595–605. PubMed PMID: 21457433.

(Review of current understanding of liver injury from herbals and dietary supplements focusing upon herbalife and hydroxycut products, green tea, usnic acid, noni juice, Chinese herbs, vitamin A and anabolic steroids; skullcap is not discussed).

Yang L, Aronsohn A, Hart J, Jensen D. Herbal hepatoxicity from Chinese skullcap: A case report. World J Hepatol. 2012;4:231–3. PubMed PMID: 22855699.

(78 year old woman developed jaundice 3 weeks after starting an herbal mixture of glucosamine, chondroitin, black catechu and Chinese skullcap [Scutellaria baicalensis] [bilirubin 7.2 mg/dL, ALT 1626 U/L, Alk P 354 U/L], resolving on stopping and recurring within 2 weeks of restarting).

Kwon H, Lee SH, Kim SE, Lee JH, Jee YK, Kang HR, Park BJ, et al. Spontaneously reported hepatic adverse drug events in Korea: multicenter study. J Korean Med Sci. 2012;27:268–73. PubMed PMID: 22379337.

(Among 9360 drug adverse reports made during 2007 and 2008 to a Korean pharmacovigilance center, 567 were hepatic of which only 3 were due to herbal medications, specific ingredients of which were not given).

Chalasani N, Vuppalanchi R, Navarro V, Fontana R, Bonkovsky H, Barnhart H, Kleiner DE, et al. Acute liver injury due to flavocoxid (Limbrel), a medical food for osteoarthritis: a case series. Ann Intern Med. 2012;156:857–60. PubMed PMID: 22711078.

(Flavocoxid, a medical food that contains Scutelleria baicalensis and Acacia catechu, was implicated in 4 cases of clinically apparent liver injury in women, ages 57 to 68 years, arising within 1-3 months of starting [bilirubin 2.0-20.8 mg/dL, ALT 741-1540 U/L, Alk P 286-770 U/L], resolving within 1-3 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, including 4 reports that mention skullcap: MacGregor [1989], Calwell [1994], Hullar [1999], Estes [2003]).

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

(Review of literature on hepatotoxicity due to herbals and dietary supplements; skullcap is mentioned, but not specifically discussed).

Dhanasekaran R, Owens V, Sanchez W. Chinese skullcap in move free arthritis supplement causes drug induced liver injury and pulmonary infiltrates. Case Reports Hepatol. 2013;2013:965092. PubMed PMID: 25431706.

(62 year old woman developed pneumonitis and jaundice 2-3 weeks after starting Move Free, a supplement that contained glucosamine, chondroitin, MSM, skullcap and black catechu [bilirubin 2.9 rising to 6.9 mg/dL, ALT 700 U/L, Alk P 250 U/L], worsening for 2 weeks and then resolving 4-8 weeks after stopping).

Björnsson ES, Bergmann OM, Björnsson HK, Kvaran RB, Olafsson S. Incidence, presentation and outcomes in patients with drug-induced liver injury in the general population of Iceland. Gastroenterology. 2013;144:1419–25. PubMed PMID: 23419359.

(In a population based study of drug induced liver injury from Iceland, 96 cases were identified over a 2 year period, including 15 [16%] due to herbal and dietary supplements, none of which were attributed to skullcap).

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 2 cases attributed to skullcap, the response to reexposure was scored as negative).

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, skullcap was not specifically implicated in any case).

Woo HJ, Kim HY, Choi ES, Cho YH, Kim Y, Lee JH, Jang E. Drug-induced liver injury: A 2-year retrospective study of 1169 hospitalized patients in a single medical center. Phytomedicine. 2015;22:1201–5. PubMed PMID: 26598920.

(Over a 2.5 year period and among 1169 hospitalized patients at a Korean medical center, 3 cases of liver injury possibly due to Scutellariae Radix were identified, all 3 hepatocellular arising after 33-48 days).

Seeff LB, Bonkovsky HL, Navarro VJ, Wang G. Herbal products and the liver: a review of adverse effects and mechanisms. Gastroenterology. 2015;148:517–532.e3. PubMed PMID: 25500423.

(Extensive review of possible beneficial as well as harmful effects of herbal products on the liver lists skullcap as a potential cause of cholestasis and acute liver failure).

Papafragkakis C, Ona MA, Reddy M, Anand S. Acute hepatitis after ingestion of a preparation of Chinese skullcap and black catechu for joint pain. Case Reports Hepatol. 2016;2016:4356749. PubMed PMID: 27144042.

(54 year old woman developed pruritus, diarrhea and jaundice 2-4 weeks after starting skullcap and black catechu for joint pains [bilirubin 12.8 mg/dL, ALT 2312 U/L, Alk P 285 U/L, INR 1.0], resolving upon stopping the supplement).

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, but does not list or discuss skullcap).

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 (Pt A): 472-501.

(Description of an online compendium of cases of liver toxicity attributed to HDS products, 2 reports of liver injury attributed to Scutellaria lateriflora [Estes 2003][Hullar 1999]).

Wong LL, Lacar L, Roytman M, Orloff SL. Urgent liver transplantation for dietary supplements: an under-recognized problem. Transplant Proc. 2017;49:322–5. PubMed PMID: 28219592.

(Among 2048 adult liver transplants recipients enrolled in the Scientific Registry of Transplant Recipients [SRTR] between 2003 and 2015, 625 were done for acute hepatic necrosis due to drug induced liver injury, half being due to acetaminophen and the 4th most frequent cause [n=21] being HDS products, but specific ingredients were not listed; skullcap is mentioned as a cause of acute liver failure as documented in the literature [Estes 2003]).

de Boer YS, Sherker AH. Herbal and dietary supplement-induced liver injury. Clin Liver Dis. 2017;21:135–49. PubMed PMID: 27842768.

(Review of the frequency, clinical features, patterns of injury and outcomes of HDS hepatotoxicity with specific mention of anabolic steroids, black cohosh, Chinese skullcap, germander, green tea, kava, pyrrolizidine alkaloids and proprietary multiingredient nutrition supplements [MINS]).

Shimada Y, Fujimoto M, Nogami T, Watari H, Kitahara H, Misawa H, Kimbara Y, Kita KI. Recurrent drug-induced liver injury caused by the incidental readministration of a Kampo Formula containing Scutellariae radix. Intern Med. 2018;57:1733–40. PubMed PMID: 29434136.

(67 year old woman had two episodes of liver injury having received different Kampo herbal regimens both of which contained Scuttellariae radix [bilirubin 1.1 and 1.3 mg/dL, ALT 139 and 880 U/L and Alk P 362 and 691 U/L], resolving rapidly each time upon stopping the herbal mixtures).

Wang ZL, Wang S, Kuang Y, Hu ZM, Qiao X, Ye M. A comprehensive review on phytochemistry, pharmacology, and flavonoid biosynthesis of Scutellaria baicalensis. Pharm Biol. 2018;56:465–84. PubMed PMID: 31070530.

(Extensive review of the chemical composition, in vitro activities of Scutellaria baicalensis with discussion of the in vitro and in vivo evidence for its potential antibacterial, antiviral, antiinflammatory, antitumor, antioxidant and hepato- and neuro-protective activities; no discussion of toxicities).

Braude MR, Bassily R. Drug-induced liver injury secondary to Scutellaria baicalensis (Chinese skullcap). Intern Med J. 2019;49:544–6. PubMed PMID: 30957370.

(51 year old man developed abdominal pain followed by jaundice 10 days after starting a herbal supplement that contained Scutellariae baicalensis [400 mg] [bilirubin 2.6 rising to 24.0 mg/dL, ALT 147 U/L, Alk P 147 U/L, INR 1.0], worsening for 3 weeks but then resolving within 12 weeks of stopping).

Puri BK, White N, Monro JA. The effect of supplementation with Scutellaria baicalensis on hepatic function. Med Hypotheses. 2019;133:109402. PubMed PMID: 31557595.

(The authors review the literature on hepatotoxicity of Scutellaria baicalensis [Chinese skullcap] and conclude that there is no convincing evidence that it causes liver injury).

Zhao T, Tang H, Xie L, Zheng Y, Ma Z, Sun Q, Li X. Scutellaria baicalensis Georgi. (Lamiaceae): a review of its traditional uses, botany, phytochemistry, pharmacology and toxicology. J Pharm Pharmacol. 2019;71:1353–69. PubMed PMID: 31236960.

(Review of the chemistry, clinical uses and toxicity of Scutellaria Baicalensis, a major ingredient in many traditional Chinese medicines, which contains more than 40 compounds including flavonoids [baicalin, mogonin], terpenoids, volatile acids and polysaccharides, used for liver protection, and treatment of diarrhea, vomiting, and high blood pressure, known as Huang Qin [yellow reed]; "there is no obvious adverse reaction in the oral preparation of Scutellaria baicalensis", but it may cause stomach discomfort, diarrhea and other minor symptoms in some patients).