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Mistletoe

Updated: July 25, 2022.

OVERVIEW

Introduction

Mistletoe is the common name for two different and unrelated plants used in traditional medicine: American mistletoe (*Phoradendron leucarpum*) and European mistletoe (*Viscum album*). American mistletoe is native to North America and is known predominantly as a Christmas decoration, but extracts of the plant have been used to treat hypotension and other disorders. European mistletoe is a parasitic vine found in Europe, Northern Africa and Southern Asia that has been used to treat headaches and seizures and more recently as therapy of cancer. Both the American and European mistletoe can be toxic in high doses, but neither has been convincingly shown to cause clinically apparent liver injury when given in conventional doses.

American Mistletoe

Background

American mistletoe (*Phoradendron leucarpum*) is an evergreen, semiparasitic plant native to North America that typically grows on poplar or apple trees and becomes prominently visible when the parasitized tree loses its leaves in winter. American mistletoe is commonly used as a Christmas decoration, but infrequently as an herbal product. The leaves, stems and berries were used in traditional medicine to treat hypotension, constipation and as an abortifacient. The active component of American mistletoe appears to be a phoratoxin which causes vasoconstriction, perhaps the basis for its purported uses. High doses can induce delirium, hallucinations, bradycardia, hypertension and cardiac arrest. Nevertheless, there have been few reports of serious complications from accidental ingestion of a up to 20 leaves or up to 5 berries of American mistletoe. Accidental ingestions are most frequent in December and occur mostly in children, but symptoms are uncommon and most children are managed as outpatients without therapy. American mistletoe is available as an oral extract in several forms and is purported to be beneficial for hypotension and constipation, but its clinical efficacy has not been shown in prospective clinical trials. There is no recommended dose. Side effects can include gastrointestinal discomfort, nausea, vomiting and drowsiness. American mistletoe is believed to be embryotoxic and an abortifacient.

Hepatotoxicity

Mistletoe in conventional oral doses is typically described as having no adverse side effects, with no mention of either hepatotoxicity or ALT elevations. Adverse events have been reported from large national registries or poison registries, but usually without details of the timing, duration and severity of the abnormalities. In the literature on mistletoe induced liver injury, the form of mistletoe (whether American or European) has rarely been documented.

Likelihood score: E (while capable of causing cardiac and neurologic toxicity in high doses, it is unlikely a cause of clinically apparent liver injury).

Other names: Golden bough, birdlime

European Mistletoe

Background

European mistletoe (*Viscum album*) is a parasitic vine that grows on several types of deciduous trees found in Europe, Northern Africa, and Southern Asia. Orally administered extracts of the leaves, stems and berries have been used in traditional medicine to treat headaches, seizures, hypertension and menopausal symptoms. The active components of European mistletoe appear to be its main glycoprotein lectins (ML-1, -2 and -3) which have antiinflammatory, immunomodulatory and antineoplastic activity in vitro. The concentrations and distribution of the main lectins vary by geographic site, the species of tree that it parasitizes, and the timing and local conditions of its harvest. Recently, purified and recombinant forms of mistletoe lectin 1 (viscumin) have been found to be a potent ribosome inactivating protein with antineoplastic activity in vitro and in animal models of cancer. Parenteral formulations of purified mistletoe lectins (viscumin, ML-1) have been developed and evaluated as a possible therapy of cancer. A recombinant form of mistletoe main lectin 1 (aviscumine) has been used extensively in Europe but was never approved for use in the United States. Randomized controlled trials of mistletoe in cancer were largely negative and used mistletoe in combination with conventional antineoplastic agents. Nevertheless, these trials demonstrated that aviscumine, even in high doses, was reasonably well tolerated. European mistletoe is not approved for therapy of any condition in the United States but products are available as dietary supplements, some of which are approved for use in Canada and the European Union. Mistletoe is available both in solution for injection and as oral tablets or capsules. In addition, It is commonly marketed in combination with other herbs, minerals and vitamins in multi-ingredient dietary supplements. Side effects can include gastrointestinal discomfort, nausea, vomiting, chills, fever, pruritus, headache and fatigue.

Hepatotoxicity

In several small, rather short term clinical trials, mistletoe in conventional oral doses was typically described as having no adverse side effects, with no mention of either hepatotoxicity or ALT elevations. Isolated reports of serum enzyme elevations during mistletoe therapy have been listed in large national registries, but usually without details of the timing, duration and severity of the abnormalities. In multiple trials of parenteral mistletoe extracts and purified or recombinant viscumin, liver injury and ALT elevations were not described. In the rare cases of clinically apparent liver injury attributed to mistletoe, the European form (*Viscum album*) was used and patients were exposed to other potential hepatotoxic herbs (skullcap, kudzu) making the role of mistletoe uncertain. Thus, mistletoe has not been shown convincingly to cause clinically apparent liver injury, at least in the doses used in humans.

Likelihood score: E (while capable of causing cardiac and neurologic toxicity in high doses, it is unlikely a cause of clinically apparent liver injury).

Other names: Birdlime, All-heal

Mechanism of Injury

The mechanism by which European mistletoe might cause liver injury is unknown, but is has biologically active glycoprotein lectins, alkaloids or monoterpene glucosides that appear to have direct toxicity that is largely cardiac.

Outcome and Management

Hepatotoxicity from mistletoe is rare and generally mild; cases have been self-limiting upon stopping the herbal.

Drug Class: Herbal and Dietary Supplements

Other names: Birdlime, All-heal

CASE REPORT

Case 1. Acute hepatocellular liver injury attributed to mistletoe.(1)

A 49 year old woman develop nausea, fatigue and abdominal discomfort several weeks after starting an herbal tablet for anxiety which was reported to be a mixture of mistletoe, skullcap, motherwort, kelp and wild lettuce. She had no history of liver disease and denied taking other medications. Laboratory tests showed a total bilirubin of 1.5 mg/dL, AST greater than 250 U/L, alkaline phosphatase 123 U/L. Tests for hepatitis B surface antigen and a cholecystogram were normal. A liver biopsy showed portal inflammation. The herbal product was stopped and she recovered slowly. Six months later, all blood tests were normal (Table). She had a recurrence of symptoms two years later and liver tests were mildly abnormal. She had restarted the herbal product, and at this point, it was implicated in causing the injury. A liver biopsy again showed portal inflammation and foci of single hepatocyte necrosis. Liver tests returned to normal after stopping the herbal product again. She then underwent a formal challenge study with the herbal tablets and rapidly developed symptoms along with rises in serum enzymes and bilirubin. Another liver biopsy showed inflammation and hepatocyte necrosis. In follow up all tests returned to normal as did liver histology as shown by another liver biopsy.

Key Points

Medication:	Herbal tablets containing mistletoe (90 mcg), kelp, motherwort, skullcap and wild lettuce: one tablet daily
Pattern:	Hepatocellular
Severity:	Mild (anicteric)
Latency:	Several weeks
Recovery:	6 months
Other medications:	None listed

Laboratory Values

Time After Starting	Time After Stopping	AST (U/L)	Alk P (U/L)	Bilirubin (mg/dL)	Other
Pre	Pre	Initiated therapy with an herbal product for anxiety			
~4 weeks	0	>250	123	2.5	Symptoms fatigue, nausea, pain
	6 months	23	55	0.8	
~4 weeks	0	62	72	0.8	Reexposure: symptoms
10 days	0	>250	144	2.2	Rechallenge: symptoms
	8 months	38	61	0.4	
	20 months	36	70	0.5	
Upper Limit of Normal		**~40**	**~100**	**1.2**	

Comment

This was the first and one of the only reports of liver injury attributed to mistletoe. While not specifically mentioned, the herb was most likely European mistletoe (*Viscum album*). Strikingly, the injury recurred on reexposure and then a formal rechallenge was conducted with liver biopsies at the time of injury as well as in recovery. While there was good evidence of recurrent injury, attribution to mistletoe has been questioned. Weakening the evidence for mistletoe being response was the lack of previous reports of any liver injury associated with its use as well as the low dose include in the tables (90 mg daily when the recommended dose was 2 to 8 grams daily. Finally, the herbal product being taken also included skullcap which has been linked to rare episodes of liver injury and might well have included other potential hepatotoxins. Finally, this report was from 1981 before the availability of tests for hepatitis A, C or E and before modern imaging techniques such as ultrasound, CT and MRI.

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Mistletoe – Generic

DRUG CLASS

Herbal and Dietary Supplements

SUMMARY INFORMATION

Fact Sheet at National Center for Complementary and Integrative Health, NIH [European]

Fact Sheet at MedlinePlus, NLM

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NUMBER	MOLECULAR FORMULA	STRUCTURE
Mistletoe	84929-55-5	Herbal	Not Applicable

CITED REFERENCE

1. Harvey J, Colin-Jones DG. Mistletoe hepatitis. Br Med J (Clin Res Ed). 1981;282(6259):186–7.

ANNOTATED BIBLIOGRAPHY

References updated: 25 July 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; several herbal medications are discussed, but not mistletoe).

Liu LU, Schiano TD. Hepatotoxicity of herbal medicines, vitamins and natural hepatotoxins. In, Kaplowitz N, DeLeve LD, eds. Drug-induced liver disease. 2nd ed. New York: Informa Healthcare USA, 2007, pp. 733-54.

(Review of hepatotoxicity of herbal and dietary supplements [HDS] published in 2007; no mention of mistletoe).

Harvey J, Colin-Jones DG. Mistletoe hepatitis. Br Med J (Clin Res Ed). 1981;282(6259):186–7.

(49 year old woman developed liver injury after taking a multi-ingredient dietary supplement containing mistletoe, skullcap, kelp, wild lettuce and motherwort [bilirubin 2.5 mg/dL, AST >250 U/L, Alk P 123 U/L], which resolved within 6 months, and had a second episode after restarting the herbal product and after recovering had another recurrence on rechallenge with the product; the authors attributed the injury to mistletoe, but the rechallenge was with the same multi-ingredient product) .

Fletcher-Hyde F. Mistletoe hepatitis. Br Med J (Clin Res Ed). 1981;282(6265):739.

(Letter in response to Harvey and Colin-Jones [1981] questioning whether the liver injury was due to mistletoe, which was used in a very low dose and has not been linked to hepatic injury previously).

Farnworth NR. Mistletoe hepatitis. Br Med J (Clin Res Ed). 1981;283(6293):1058.

(Letter in response to Harvey and Colin-Jones [1981] questioning whether the liver injury was due to mistletoe, mentioning that none of the ingredients in the product have been linked to liver injury in animals or humans so that the product might have contained a contaminant that was hepatotoxic).

Baleful mistletoe. Lancet. 1982;2(8313):1442. PubMed PMID: 6129516.

(Editorial on the report of Harvey and Colin-Jones [1981] and the subsequent controversy about its hepatotoxin potential refers to it as Viscum album, the European variety).

Stirpe F. Mistletoe toxicity. Lancet. 1983;1(8319):295. PubMed PMID: 6130311.

(Letter in response to Lancet editorial [1982] mentioning that mistletoe contains a toxin lectin called viscumin which varies in concentration among different mistletoe leaves and has unknown but suspected toxicity for humans).

Hall AH, Spoerke DG, Rumack BH. Assessing mistletoe toxicity. Ann Emerg Med. 1986;15:1320–3. PubMed PMID: 2877602.

(Among 14 instances of mistletoe ingestion in children from the Rocky Mountain Poison and Drug Center between 1982 and 1985, none became symptomatic and most received no treatment except for ipecac; and review of 318 cases reported to National Poison Control centers, 87% were asymptomatic, 2% had mild effects, only one was considered moderate, and none resulted in serious injury or death).

Bruseth S, Enge A. Scullcap--leverskade. Misteltein og leverskade. Tidsskr Nor Laegeforen. 1992;112:2389–90. [Scullcap-liver damage and mistletoe hepatitis]. Norwegian.

(Letter in response to the publication on mistletoe hepatitis by Harvey and Colin-Jones [1981] suggests that it was actually due to skullcap, which has been reported to cause liver injury).

Spiller HA, Willias DB, Gorman SE, Sanftleban J. Retrospective study of mistletoe ingestion. J Toxicol Clin Toxicol. 1996;34:405–8. PubMed PMID: 8699554.

(Among 92 episodes of mistletoe exposure reported to 3 regional poison control centers between 1990 and 1993, only 11 [12%] were associated with symptoms including gastrointestinal upset in 6, mild drowsiness in 2, and 1 case each of eye irritation, ataxia and seizure; were no permanent injuries or deaths).

Krenzelok EP, Jacobsen TD, Aronis J. American mistletoe exposures. Am J Emerg Med. 1997;15:516–20. PubMed PMID: 9270395.

(Analysis of 1754 exposures to American mistletoe reported to American Poison control centers, 96% were asymptomatic, 92% occurred in children, and less than 1% had any signs of toxicity).

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 oil [1], skullcap [2], Chinese herbs [9], valerian [1]; mistletoe is not listed]).

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 attributed to herbal products, including Ma huang, usnic acid, kava, chaparral and skullcap; but none were attributed to mistletoe).

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 found 14 attributed to European mistletoe, which were mostly anaphylactoid reactions, fever and irritability; mistletoe was not listed as an agent with liver-related adverse events).

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, including several herbal mixtures, usnic acid, Ma Huang, black cohosh, and Hydroxycut, but not mistletoe).

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; mistletoe is not discussed).

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 the report of mistletoe hepatitis by Harvey and Colin-Jones).

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, 15 of which [16%] were attributed to HDS products, but none were listed as containing mistletoe).

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 does not discuss mistletoe).

Navarro VJ, Seeff LB. Liver injury induced by herbal complementary and alternative medicine. Clin Liver Dis. 2013;17:715–35. PubMed PMID: 24099027.

(Review of the epidemiology, regulatory status, diagnosis, pathogenesis and causes of liver injury from herbal products with specific discussion of conjugated linoleic acid, ephedra, germander, green tea, usnic acid,

flavocoxid, aloe vera, chaparral, greater celandine, black cohosh, comfrey, kava, skullcap, valerian, noni juice, pennyroyal and traditional herbal remedies).

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 839 cases of liver injury from drugs collected in the US between 2004 and 2013, 130 were due to HDS products, including 45 from body building agents [probably anabolic steroids] and 85 from diverse HDS products none of which were reported as containing mistletoe).

Navarro VJ, Lucena MI. Hepatotoxicity induced by herbal and dietary supplements. Semin Liver Dis. 2014;34:172–93. PubMed PMID: 24879982.

(Review of the international regulatory framework for HDS products and the epidemiology, clinical presentation, diagnosis and cause of HDS associated liver injury with tables and discussion of the most commonly implicated agents, but does not include mention of mistletoe).

Kim HJ, Kim H, Ahn JH, Suk HJ. Liver injury induced by herbal extracts containing mistletoe and kudzu. J Altern Complement Med. 2015;21:180–5. PubMed PMID: 25668233.

(55 year old Korean man developed fever, abdominal pain and dark urine 1 month after starting a mistletoe extract and 10 days after starting a kudzu root extract [bilirubin 6.3 mg/dL, ALT 1528 U/L, Alk P 160 U/L, INR 1.14], all symptoms resolving and abnormal enzyme levels falling to normal within a week of stopping).

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 herbal associated liver injury does not discuss mistletoe specifically).

Dohmen W, Breier M, Mengs U. Cellular immunomodulation and safety of standardized aqueous mistletoe extract PS76A2 in tumor patients treated for 48 weeks. Anticancer Res. 2004;24:1231–7. PubMed PMID: 15154652.

(Among 12 adults with various cancers treated with mistletoe lectin subcutaneously twice weekly for 48 weeks, NK cells increased and therapy was well tolerated by all patients, ALT and AST levels remaining normal).

Schöffski P, Riggert S, Fumoleau P, Campone M, Bolte O, Marreaud S, Lacombe D, et al; European Organization for Research and Treatment of Cancer New Drug Development Group. Phase I trial of intravenous aviscumine (rViscumin) in patients with solid tumors. Ann Oncol. 2004;15:1816–24. PubMed PMID: 15550588.

(Among 41 patients with advanced refractory solid malignancies treated in a phase 1 dose escalation study of aviscumine [recombinant mistletoe lectin 1] given intravenously twice weekly, adverse events arose with high doses including fatigue, fever, nausea and vomiting, allergic reactions and reversible elevations in serum ALT, AST and alkaline phosphatase).

Augustin M, Bock PR, Hanisch J, Karasmann M, Schneider B. Safety and efficacy of the long-term adjuvant treatment of primary intermediate- to high-risk malignant melanoma (UICC/AJCC stage II and III) with a standardized fermented European mistletoe (Viscum album L.) extract. Results from a multicenter, comparative, epidemiological cohort study in Germany and Switzerland. Arzneimittelforschung. 2005;55:38–49. PubMed PMID: 15727163.

(Among 329 patients with advanced malignant melanoma treated with fermented European mistletoe subcutaneously 2 to 3 times weekly for at least 3 months, adverse events were uncommon [11%] and included fatigue, fever, allergic reactions and itching; no mention of ALT elevations or hepatotoxicity).

Courtemanche J, Peterson RG. Beware the mistletoe. CMAJ. 2006;175:1523–4. PubMed PMID: 17146088.

(Commentary on the potential toxicity of house plants, particularly for toddlers and children who might try to eat them, including mistletoe berries which can cause severe nausea and vomiting).

Melzer J, Iten F, Hostanska K, Saller R. Efficacy and safety of mistletoe preparations (Viscum album) for patients with cancer diseases. A systematic review. Forsch Komplementmed. 2009;16:217–26. PubMed PMID: 19729932.

(Systematic review of the literature on mistletoe therapy of cancer identified 18 clinical trials in approximately 6800 patients, overall found little evidence of antineoplastic activity but seemed to improve quality of life; side effect arise in 17.5% of patients but are generally mild-to-moderate and include fatigue, fever, headache, itching and local reactions with one serious event of angioedema; no mention of ALT elevations or hepatotoxicity).

Steele ML, Axtner J, Happe A, Kröz M, Matthes H, Schad F. Adverse drug reactions and expected effects to therapy with subcutaneous mistletoe extracts (Viscum album L.) in cancer patients. Evid Based Complement Alternat Med. 2014;2014:724258. PubMed PMID: 24672577.

(Among 1923 patients with cancer who received complementary therapy using mistletoe extract, 14.7% had an adverse reaction, which were mostly mild-to-moderate and included headache, fatigue, fever, local reactions and itching; no mention of ALT elevations or hepatotoxicity).

Freuding M, Keinki C, Micke O, Buentzel J, Huebner J. Mistletoe in oncological treatment: a systematic review: Part 1: survival and safety. J Cancer Res Clin Oncol. 2019;145:695–707. PubMed PMID: 30673873.

(Systematic review of the literature on efficacy of mistletoe in cancer identified 28 publications with a total of 2639 patients with various forms of advanced cancer, mistletoe was usually added to conventional therapy, and while most studies were of low quality, overall there was no evidence that mistletoe therapy had any effect on survival; side effects were usually mild and self-limited and serious adverse events were rare; no mention of ALT elevations or hepatotoxicity).

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 mistletoe as being implicated in only one report [Harvey and Colin-Jones 1981] in a patient also taking skullcap, a known hepatotoxin).

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], while none were attributed to mistletoe).

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], but none were attributed to mistletoe).

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 [91], green tea [90] Herbalife products [64], kava kava [62] and greater celandine [48]; mistletoe was implicated in 3 cases but details were not provided).