



Polygonum Multiflorum

Updated: August 18, 2020.

OVERVIEW

Introduction

Polygonum multiflorum is an herb native to China, extracts of which has been used for centuries as a treatment for a wide range of conditions including backache, dizziness, liver disease, graying of the hair and constipation. *P. multiflorum* is also known as Shou Wu Pian, He Shou Pian, Fo-Ti and Chinese knotweed. *Polygonum multiflorum* has been implicated in numerous reports of clinically apparent acute liver injury which can be severe and even fatal.

Background

Polygonum multiflorum is a commonly used and ancient Chinese herbal remedy prepared from the root of the tuber, *Polygonum multiflorum*, known as the Chinese climbing knotweed (Fo Ti). Fo Ti is a plant native to China which has been cultivated widely elsewhere, including the United States. Extracts of the roots of *Polygonum multiflorum* have been used for centuries in traditional Chinese medicine for a multitude of conditions and as an agent to prevent aging. Some of the historical uses include cancer, tuberculosis, diabetes, hypertension, infections, erectile dysfunction, infertility, and muscle soreness. It is also used as a tonic in liver and kidney conditions and to fortify muscles and bones. The extract has been marketed as a pill and claimed to be beneficial for headache, dizziness, graying of the hair, constipation and liver disease. *Polygonum multiflorum* can also be brewed in teas, and extracts are used in topical creams or ointments for skin conditions and muscle soreness. The efficacy of *Polygonum multiflorum* has not been proven in prospective, controlled trials but it is widely available over the counter. The active components of *Polygonum multiflorum* are believed to be anthraquinones including chrysophanol, emodin and rhein. Anthraquinones may also account for its effect in constipation but may also account for its hepatotoxicity. Various oral formulations are available, and it is also taken as a tea using extracts of dried *Polygonum* roots. Common side effects are abdominal pain, diarrhea, nausea and vomiting. Serious adverse events are rare, although hepatotoxicity has been increasingly reported, particularly from China and East Asia.

Hepatotoxicity

Several published cases and a large case series from China, Korea and Japan of clinically apparent acute liver injury have been attributed to use of *Polygonum multiflorum*. Indeed, in China *Polygonum multiflorum* is reported to be the most common cause of herbal product related liver injury. The latency to onset is usually short, but ranges from a few days to as long as 6 months. The pattern of serum enzyme elevations is typically hepatocellular or mixed and the clinical presentation resembles acute viral hepatitis with onset of fatigue, nausea and right upper quadrant pain followed by dark urine and jaundice. Immunoallergic features are uncommon as

are autoantibodies. Liver biopsy shows changes typical of acute hepatitis. The course is usually self-limited, resolving rapidly once the herbal is discontinued, but up to 10% of clinically apparent cases have been fatal or led to urgent liver transplantation. Recurrence upon re-exposure with a more rapid time to onset has been reported. Recent case series have identified the HLA allele B*35:01 as a risk factor, being found in 70% to 88% of cases compared to 5% of controls in Chinese populations. A similar HLA-association has been found for green tea in the United States.

Likelihood score: A (well established cause of clinically apparent liver injury).

Mechanism of Injury

The mechanism of hepatotoxicity of *Polygonum multiflorum* is not known, but the injury is usually attributed to the anthraquinones (such as emodin) which are major constituents in *Polygonum multiflorum*. In a single report, the major compound identified in the recovered tablets was a stilbene glycoside, tetrahydroxystilbene-glucopyranoside. The HLA allele B*35:01 appears to be a major risk factor for liver injury from *Polygonum multiflorum* suggesting that the injury is immunologically mediated.

Outcome and Management

Hepatotoxicity from *Polygonum multiflorum* is usually self-limited but can be prolonged and is occasionally fatal. Recurrence with restarting the herb is common and rechallenge should be avoided. There is little evidence for cross sensitivity to the hepatotoxic effects of other herbal medications. Use of corticosteroids has not been reported to be effective.

Other Names: Fo Ti, Chinese climbing knotweed, Fleece-flower root, Chinese cornbind, Ho Shou Wu, Shou Wu Pian, Shen Min, Zi Shou Wu

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

Other herbals in the Subclass: [Chinese and Other Asian Herbal Medicines](#)

CASE REPORT

Case 1. Recurrent hepatitis due to Shou Wu Pian.(1)

A 5 year old girl developed jaundice and dark urine 4 months after her parents started her on Shou Wu Pian (3 tablets daily) for hair loss. She was otherwise healthy, with normal growth and development and no history of liver disease or risk factors for viral hepatitis. She was taking no conventional medications and her family initially did not mention the herbal use. Physical examination showed jaundice and mild hepatomegaly without fever, rash, abdominal tenderness or splenomegaly. Laboratory results showed raised serum bilirubin levels (4.9 mg/dL), and elevations in serum aminotransferases (ALT 1543 U/L, AST 1938 U/L) and gamma-glutamyl transpeptidase levels (GGT 67, normal <17 U/L). Tests for hepatitis A, B and C were negative as were tests for cytomegalovirus and Epstein Barr virus infection. Abdominal ultrasound showed normal liver and biliary tract. Liver tests improved without specific therapy and one month later liver tests were normal (Table). However, she returned with recurrence of jaundice 2 months later and at this point the history of herbal use was obtained. After recovering from the initial liver injury, the Shou Wu Pian had been restarted at a lower dose (2 tablets per day) and she redeveloped jaundice within a month of restarting. She again began to improve once the herbal medication was stopped, but liver test abnormalities did not completely resolve until 5 months later. Analysis of residual tablets of the Shou Wu Pian demonstrated the stilbene glycoside, tetrahydrostilbene-glucopyranoside, as the major constituent with only trace amounts of anthraquinones.

Key Points

Medication:	Shou Wu Pian (3 tablets daily)
Pattern:	Hepatocellular (R=9.8, using GGT instead of alkaline phosphatase)
Severity:	3+ (jaundice, hospitalization)
Latency:	16 weeks initially, 4 weeks on re-exposure
Recovery:	4 weeks initially, 21 weeks on re-exposure
Other medications:	None

Laboratory Values

Time After Starting	Months After Stopping	ALT (U/L)	Alk P (U/L)	Bilirubin (mg/dL)	Comments
		Shou Wu Pian taken for hair loss for 4 months			
4 months	0	1543	67	4.9	
5 months	1 months	50	21	0.4	
		Shou Wu Pian restarted for 1 month			
7 (1) months	0	1277	98	3.7	
2 months	1 months	65	23	0.5	
6 months	5 months	35	9	0.5	
Normal Values		<40	<17	<1.2	

Comment

The case history is somewhat typical of herbal induced liver injury, in that the family did not inform the physicians that the child was receiving Shou Wu Pian (Polygonum multiflorum) and did not consider it harmful or imagine that it was the cause of the hepatitis. The clinical features resembled acute hepatitis, but the recurrence (with a shorter latency) on restarting the herbal makes this a convincing case for Polygonum multiflorum induced acute liver injury.

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Shou Wu Pian – Generic

DRUG CLASS

Herbal and Dietary Supplements

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Shou Wu Pian – Generic

DRUG CLASS

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CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NUMBER	MOLECULAR FORMULA	STRUCTURE
Shou Wu Pian	No Information	Herbal mixture	Not applicable

CITED REFERENCE

1. Panis B, Wong DR, Hooymans PM, De Smet PAMG, Rosias PPR. Recurrent toxic hepatitis in a Caucasian girl related to the use of Shou-Wu-Pian, a Chinese herbal preparation. *J Pediatr Gastroenterol Nutr.* 2005;41:256–8. PubMed PMID: 16056110.

ANNOTATED BIBLIOGRAPHY

References updated: 15 August 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 Chinese herbal products and teas are discussed generally without focus on Shou Wu Pian).*
- 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] discusses Chinese and other Asian herbal medicines including Shou Wu Pian [Polygonum multiflorum]).*
- Carlsson C. Herbs and hepatitis. *Lancet.* 1990;336:1068. PubMed PMID: 1977040.
- (Analysis of laboratory results from 395 patients found higher ALT levels among 53 patients taking herbals [55 U/L] than among those who did not [12 U/L]).*
- But PP, Tomlinson B, Lee KL. Hepatitis related to the Chinese medicine Shou-wu-pian manufactured from *Polygonum multiflorum*. *Vet Hum Toxicol.* 1996;38:280–2. PubMed PMID: 8829347.
- (31 year old woman from Hong Kong developed jaundice several weeks after starting Shou Wu Pian for hair loss [bilirubin 4.0 rising to 6.1 mg/dL, ALT 870 U/L, Alk P 108 U/L], resolving within 3 weeks of stopping).*
- Park GJH, Mann SP, Ngu MC. Acute hepatitis induced by Shou-Wu-Pian, a herbal product derived from *Polygonum multiflorum*. *J Gastroenterol Hepatol.* 2001;16:115–7. PubMed PMID: 11206309.
- (46 year old woman developed pruritus and jaundice 2 weeks after starting Shou Wu Pian [bilirubin 12.6 mg/dL, ALT 876 U/L, Alk P 185 U/L], resolving within a month of stopping).*
- De Smet PAGM. Herbal remedies. *N Engl J Med.* 2002;347:2046–56. PubMed PMID: 12490687.
- (Review of status and difficulties of herbal medications including lack of standardization, federal regulation, contamination, safety, hepatotoxicity and drug-herb interactions; specific discussion of 4 herbs with therapeutic promise: ginkgo, hawthorn, saw palmetto and St. John's wort).*
- Ernst E. Adulteration of Chinese herbal medicines with synthetic drugs: a systematic review. *J Intern Med.* 2002;252:107–13. PubMed PMID: 12190885.

(Systematic review of literature on adulteration of herbals with conventional medications, in 15 case reports and 2 cases series of 21 patients; contaminants included NSAIDs, corticosteroids, benzodiazepines, diuretics and antidiabetic medications, in up to 24% of products).

Mazzanti G, Battinelli L, Daniele C, Mastroianni CM, Lichtner M, Coletta S, Costantini S. New case of acute hepatitis following the consumption of Shou Wu Pian, a Chinese herbal product derived from Polygonum multiflorum. *Ann Intern Med.* 2004;140:W30. PubMed PMID: 15069011.

(78 year old man developed jaundice 1 month after starting Shou Wu Pian for chronic prostatitis [bilirubin 25.5 mg/dL, ALT 1276 U/L, Alk P 409 U/L], resolving rapidly upon stopping).

Panis B, Wong DR, Hooymans PM, De Smet PAMG, Rosias PPR. Recurrent toxic hepatitis in a Caucasian girl related to the use of Shou-Wu-Pian, a Chinese herbal preparation. *J Pediatr Gastroenterol Nutr.* 2005;41:256–8. PubMed PMID: 16056110.

(5 year old girl developed jaundice 4 months after being started on Shou Wu Pian [bilirubin 4.9 mg/dL, ALT 1543 U/L, Alk P normal], resolving within 5 weeks and recurring within 4 weeks of restarting, resolving this second time only after 5 months: Case 1).

Yuen MF, Tam S, Fung J, Wong DK, Wong BC, Lai CL. Traditional Chinese medicine causing hepatotoxicity in patients with chronic hepatitis B infection: a 1-year prospective study. *Aliment Pharmacol Ther.* 2006;24:1179–86. PubMed PMID: 17014576.

(Among 45 patients from Hong Kong with chronic hepatitis B who had an acute exacerbation of disease, the cause appeared to be an exacerbation of hepatitis B in 28, acute hepatitis A in 2, acute hepatitis E in 3, conventional drug induced liver injury in 3, alcohol in 2 and use of Traditional Chinese Medicines in 7, one of whom had been taking Polygonum multiflorum for weight loss for 6 weeks and developed a severe hepatitis, ultimately requiring liver transplantation).

Cárdenas A, Restrepo JC, Sierra F, Correa G. Acute hepatitis due to Shen-Min: a herbal product derived from Polygonum multiflorum. *J Clin Gastroenterol.* 2006;40:629–32. PubMed PMID: 16917407.

(28 year old woman developed fatigue followed by jaundice 8 weeks after starting Shen-Min for hair loss [bilirubin 12.3 mg/dL, ALT 2922 U/L, Alk P 153 U/L], resolving within 4 weeks of stopping the herbal).

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

(Review of herbal induced hepatotoxicity, with a review of Chinese herbal medicines such as Chaso, Onshido, Sho-Saiko-To, Jin Bu Huan, Ma Huang and Shou Wu Pian).

Chitturi S, Farrell GC. Hepatotoxic slimming aids and other herbal hepatotoxins. *J Gastroenterol Hepatol.* 2008;23:366–73. PubMed PMID: 18318821.

(Review of hepatotoxicity of herbal medications focusing upon those used for weight loss, including nitrosfenfluramine, usnic acid, ephedra, germander, skullcap and green tea; other herbs discussed include Shou Wu Pian).

Laird AR, Ramchandani N, deGoma EM, Avula B, Khan IA, Gesundheit N. Acute hepatitis associated with the use of an herbal supplement (Polygonum multiflorum) mimicking iron-overload syndrome. *J Clin Gastroenterol.* 2008;42:861–2. PubMed PMID: 18580499.

(35 year old man developed jaundice “several months” after starting “NuHair” [containing Polygonum multiflorum] for hair loss [bilirubin 4.6 rising to 13.7 mg/dL, ALT 2714 U/L, Alk P 137 U/L, INR 1.3], resolving 4 months after stopping).

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. PubMed PMID: 19159172.

(Among 521 cases of drug induced liver injury submitted to Spanish registry, 13 [2%] were due to herbals, including *Camellia sinensis*, *Cassia angustifolia*, kava, valerian, *Rhamnus purshianus*, fitosoja, biosoja, *Aesculus hippocatanum*, chitosan, *Couterea latifloral*; no mention of *Polygonum multiflorum*).

Chalasanani 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 herbals or dietary supplements [HDS] but none specifically to Sho Wu Pian or a *Polygonum multiflorum* containing product).

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 including traditional Chinese herbal medicines and usnic acid).

Wang YP, Shi B, Chen YX, Su J, Jiang CF, Xie WF. Drug-induced liver disease: an 8 year study of patients from one gastroenterological department. *J Dig Dis*. 2009;10:195–200. PubMed PMID: 19659787.

(Among 30 patients with drug induced liver disease seen at a single medical university in Shanghai between 2000-2008, 12 cases were attributed to Chinese herbs, but specific agents not discussed, 9 were jaundiced, 6 hepatocellular, 3 cholestatic and 2 mixed enzyme pattern elevations).

Cho HC, Min HJ, Ha CY, Kim HJ, Kim TH, Jung WT, Lee OJ, Bae IG. Reactivation of pulmonary tuberculosis in a patient with *Polygonum multiflorum* Thunb-induced hepatitis. *Gut Liver*. 2009;3:52–6. PubMed PMID: 20479902.

(34 year old man developed jaundice 30 days after starting daily use of *Polygonum multiflorum* tea and extract [bilirubin 25.3 mg/dL, ALT 1452 U/L, Alk P 111 U/L] with neutropenia [and pulmonary tuberculosis], liver injury resolving slowly after stopping herbal product).

Furukawa M, Kasajima S, Nakamura Y, Shouzushima M, Nagatani N, Takinishi A, Taguchi A, et al. Toxic hepatitis induced by show-wu-pian, a Chinese herbal preparation. *Intern Med*. 2010;49:1537–40. PubMed PMID: 20686286.

(53 year old Japanese woman developed fatigue after taking Sho Wu Pian for 8 months [bilirubin 1.2 mg/dL, ALT 417 U/L, Alk P 1425 U/L, ANA 1:320], resolving within 2 months of stopping).

Valente G, Sanges M, Campione S, Bellevicine C, De Franchis G, Sollazzo R, Mattera D, et al. Herbal hepatotoxicity: a case of difficult interpretation. *Eur Rev Med Pharmacol Sci*. 2010;14:865–70. PubMed PMID: 21222373.

(35 year old Italian woman developed fatigue, abdominal pain and jaundice 4 weeks after starting 3 herbal products for hair loss including Sho Wu Pian [*Polygonum multiflorum*], glycyrrhizin and black cohosh [bilirubin 3.3 mg/dL, ALT 1540 U/L, Alk P 1020 U/L, normal INR], resolving within 2 months of stopping).

Bae SH, Kim DH, Bae YS, Lee KJ, Kim DW, Yoon JB, Hong JH, Kim SH. Korean J Hepatol. 2010;16:182–6. [Toxic hepatitis associated with *Polygonum multiflorum*]. PubMed PMID: 20606503.

(54 year old Korean woman developed fatigue 1 month after starting Sho Wu [ALT 1136 U/L, Alk P 324 U/L], resolving rapidly but recurring upon re-exposure).

Jung KA, Min HJ, Yoo SS, Kim HJ, Choi SN, Ha CY, Kim HJ, et al. Drug-Induced Liver Injury: Twenty five cases of acute hepatitis following ingestion of *Polygonum multiflorum* Thunb. *Gut Liver*. 2011;5:493–9. PubMed PMID: 22195249.

(Case series of 25 patients with suspected hepatotoxicity from Polygonum multiflorum seen between 2007 and 2009 at a single Korean hospital; ages 24 to 65 years, presenting with jaundice after taking herbal as a tea or liquid extract for 2 to 180 days [bilirubin 1.6-32.9 mg/dL, ALT 271-1706 U/L, Alk P 81-465 U/L], injury pattern being hepatocellular [n=18] or mixed [n=7], liver biopsies showing acute hepatocellular injury, resolving in most, one patient died, one underwent liver transplantation, and one had recurrence on re-exposure).

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; Shou Wu Pian and Polygonum multiflorum not discussed).

Banarova A, Koller T, Payer J. Toxická hepatitída po Polygonum multiflorum. *Vnitr Lek.* 2012;58:958–62. [Toxic hepatitis induced by Polygonum multiflorum]. Slovak. PubMed PMID: 23691566.

(33 year old woman developed nausea and jaundice 4 weeks after starting Polygonum multiflorum [bilirubin 6.1 mg/dL, ALT 1163 U/L, Alk P 131 U/L], resolving within 4 weeks of stopping).

Cortez E, Boulger C, Bernard A. Ban Tu Wan hepatotoxicity. *BMJ Case Rep.* 2012;2012:bcr2012006438. PubMed PMID: 22878995.

(Middle aged Asian-American woman developed fatigue and confusion 2-3 months after starting an herbal mixture called Ban Tu Wan for hair loss [bilirubin 4.1 mg/dL, ALT 5386 U/L, Alk P 199 U/L], with coagulopathy and renal dysfunction progressing to hepatic failure and death within a few days; Ban Tu Wan was labelled as having 9 botanical ingredients including Polygonum multiflorum).

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 four reports of injury due to Polygonum multiflorum: Ho Shou Wu [Bae 2010], Shen Min [Cardenas 2006], and Shou Wu Pian [Jung 2011 and Panis 2005]).

Teschke R. Traditional Chinese Medicine induced liver injury. *J Clin Transl Hepatol.* 2014;2:80–94. PubMed PMID: 26357619.

(Review of literature on hepatotoxicity of traditional Chinese Medicines includes mention of cases attributed to Polygonum multiflorum and multiple products that include it: Shou Wu Pian, Shen Min, Ban Tu Wan and Ho Shou Wu).

Dong H, Slain D, Cheng J, Ma W, Liang W. Eighteen cases of liver injury following ingestion of Polygonum multiflorum. *Complement Ther Med.* 2014;22:70–4. PubMed PMID: 24559819.

(Among 18 patients with Polygonum multiflorum [Fo-Ti] hepatotoxicity seen at a Chinese referral center between 2005 and 2012, median age was 42 years, latency 27 days [range 1-120 days], 16 [89%] with jaundice, all hepatocellular [ALT 601 to 4095 U/L, Alk P 89 to 816 U/L], all recovered and none died; frequently ingested as a decoction with alcohol or as a tea).

Ma KF, Zhang XG, Jia HY. CYP1A2 polymorphism in Chinese patients with acute liver injury induced by Polygonum multiflorum. *Genet Mol Res.* 2014;13:5637–43. PubMed PMID: 25117321.

*(Among 43 cases of Polygonum multiflorum hepatotoxicity tested for CYP1A2 variants, 47% of cases vs 28% of controls had CYP 1A2*1C, a variant associated with reduced activity).*

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, four were due to unnamed Chinese herbs but none were attributed specifically to *Polygonum multiflorum*, Fo-Ti or Shou Wu Pian).
- Teschke R, Zhang L, Long H, Schwarzenboeck A, Schmidt-Taenzer W, Genthner A, Wolff A, et al. Traditional Chinese medicine and herbal hepatotoxicity: a tabular compilation of reported cases. *Ann Hepatol*. 2015;14:7–19. PubMed PMID: 25536637.
- (Review of literature on hepatotoxicity of traditional Chinese Medicines includes details of the 25 cases attributed to *Polygonum multiflorum* published by Jung et al [2011]).
- Zhu Y, Li YG, Wang JB, Liu SH, Wang LF, Zhao YL, Bai YF, et al. Causes, features, and outcomes of drug-induced liver injury in 69 children. *Gut Liver*. 2015;9:525–33. PubMed PMID: 25717050.
- (Among 69 children hospitalized for drug induced liver injury between 2009 and 2012, the most frequent causes were antibiotics [n=18] and Chinese Traditional Medicines [n=15] including 3 cases due to *Polygonum multiflorum*).
- Bounda GA, Feng YU. Review of clinical studies of *Polygonum multiflorum* Thunb. and its isolated bioactive compounds. *Pharmacognosy Res*. 2015;7:225–36. PubMed PMID: 26130933.
- (Review of the preparation, chemical constituents, pharmacology, clinical efficacy and hepatotoxicity of *Polygonum multiflorum*).
- Li X, Qu C, He Q, Chen W, Zhang X, Liu X, Liu Y, et al. Acute hepatitis induced by a Chinese herbal product Qibao Meiran Wan: a case study. *Int J Clin Exp Med*. 2015;8:11624–7. PubMed PMID: 26379995.
- (26 year old Chinese man developed fatigue followed by jaundice one month after starting Qibao Meiran Wan for hair growth [bilirubin 3.2 mg/dL, ALT 1674 U/L, Alk P 110 U/L], resolving within a month of stopping the herbal product which was labelled as containing 8 different botanicals, one of which was *Polygonum multiflorum*).
- Douros A, Bronder E, Andersohn F, Klimpel A, Kreutz R, Garbe E, Bolbrinker J. Herb-Induced Liver Injury in the Berlin Case-Control Surveillance Study. *Int J Mol Sci*. 2016;17:E114. pii. PubMed PMID: 26784183.
- (Among 198 patients with suspected drug induced liver injury seen at Berlin Hospitals and enrolled in a prospective database, 10 were attributed to herbal supplements but none were attributed to Shou Wu Pian or *Polygonum multiflorum*).
- 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 8 cases of jaundice and “numerous” cases of hepatitis associated with *Polygonum multiflorum* and Shou Wu Pian).
- Li H, Wang X, Liu Y, Pan D, Wang Y, Yang N, Xiang L, et al. Hepatoprotection and hepatotoxicity of Heshouwu, a Chinese medicinal herb: Context of the paradoxical effect. *Food Chem Toxicol*. 2017;108:407–418. PubMed PMID: 27484243.
- (Review of the methods of preparation and in vivo and in vitro effects of two forms of *Polygonum multiflorum*—Sheng Shou Wu [dried roots] and Zhi He Shou Wu [boiled roots with black soybean] used in Traditional Chinese Medicine which have different concentrations of basic constituents and have both hepatoprotective and hepatotoxic potential).
- Li CY, He Q, Gao D, Li RY, Zhu Y, Li HF, Feng WW, et al. Idiosyncratic drug-induced liver injury linked to *Polygonum multiflorum*: A case study by pharmacognosy. *Chin J Integr Med*. 2017;23:625–30. PubMed PMID: 28523534.

- (41 year old man developed fatigue 2 weeks after starting Polygonum multiflorum for blackening of his hair followed in a week by jaundice [bilirubin 9.6 mg/dL, ALT 766 U/L, Alk P 132 U/L, INR 1.1], resolving within a month of stopping the product which tested positive for the herb).*
- Wang Y, Wang L, Saxena R, Wee A, Yang R, Tian Q, Zhang J, et al. Clinicopathological features of He Shou Wu-induced liver injury: This ancient anti-aging therapy is not liver-friendly. *Liver Int.* 2019;39:389–400. PubMed PMID: 30066422.
- (Among 547 patients hospitalized for drug induced liver injury, 29 cases were attributed to He Shou Wu [Polygonum multiflorum] all of which were hepatocellular with median initial bilirubin of 6.0 mg/dL, ALT 995 U/L, Alk P 165 U/L, median latency of 40 days [range 4-300], 79% were jaundiced, 86% recovered, 1 recurred on rechallenge, 2 had chronic injury and 1 [3%] died).*
- Jing J, Wang RL, Zhao XY, Zhu Y, Niu M, Wang LF, Song XA, et al. Association between the concurrence of pre-existing chronic liver disease and worse prognosis in patients with an herb- “Polygonum multiflorum” thunb. induced liver injury: a case-control study from a specialised liver disease center in China. *BMJ Open.* 2019;9:e023567. PubMed PMID: 30782709.
- (Among 5703 patients hospitalized for drug induced liver injury, 145 were attributed to Polygonum multiflorum, among whom those with preexisting liver disease [n=33: 23%] had a higher mortality rate [9% vs 1%]).*
- Liu Y, Wang W, Sun M, Ma B, Pang L, Du Y, Dong X, Yin X, Ni J. "Polygonum multiflorum"-induced liver injury: clinical characteristics, risk factors, material basis, action mechanism and current challenges. *Front Pharmacol.* 2019;10:1467. PubMed PMID: 31920657.
- (Review of the clinical uses and hepatotoxicity of Polygonum multiflorum also called Ho Shou Wu in China which is used for detoxification and bowel relaxation and which “tonifies the liver and kidney” and benefits “black beard”).*
- Li C, Rao T, Chen X, Zou Z, Wei A, Tang J, Xiong P, et al. HLA-B*35:01 allele Is a potential biomarker for predicting Polygonum multiflorum-Induced liver injury in humans. *Hepatology.* 2019;70:346–57. PubMed PMID: 30985007.
- (Among 26 cases of Polygonum multiflorum hepatotoxicity 88% had at least one copy of the HLA-B*35:01 allele compare to 12% of 33 patients with other forms of drug induced liver injury and 5% of normal controls).*
- Aithal GP. Of Potions, poisons, Polygonum, and pre-emptive polymorphism. *Hepatology.* 2019;70:8–10. PubMed PMID: 31155733.
- (Editorial in response to Li [2019]).*
- Zhang L, Niu M, Wei AW, Tang JF, Tu C, Bai ZF, Zou ZS, et al. Risk profiling using metabolomic characteristics for susceptible individuals of drug-induced liver injury caused by Polygonum multiflorum. *Arch Toxicol.* 2020;94:245–56. PubMed PMID: 31630224.
- (Metabolomics identified 25 metabolites in pretreatment serum that separated 6 Polygonum multiflorum treated subjects who developed evidence of hepatotoxicity from 30 who tolerated therapy, the metabolites being involved in glycerophospholipid, sphingolipid, fatty acid, histidine and aromatic amino acid metabolic pathways).*
- Yang WN, Pang LL, Zhou JY, Qiu YW, Miao L, Wang SY, Liu XZ, et al. Single-nucleotide polymorphisms of HLA and Polygonum multiflorum-induced liver injury in the Han Chinese population. *World J Gastroenterol.* 2020;26:1329–39. PubMed PMID: 32256020.
- (Use of single-nucleotide polymorphisms identified HLA-B*35:01 to be associated with 73 cases of polygonum multiflorum hepatotoxicity [allele frequency 0.41] compared to 118 cases of other drug induced liver injury [0.12] and to Han population controls [0.027]).*