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Chaparral

Updated: January 23, 2017.

OVERVIEW

Introduction

Chaparral is a botanical extract of the woody shrub known as creosote bush (Larrea tridentata) which has antioxidant activity and is claimed to have beneficial effects for many conditions from skin rash to cancer. Chaparral extracts have been linked to several cases of clinically apparent liver injury, some of which have led to acute liver failure and need for emergency liver transplantation.

Background

Chaparral is prepared from the leaves of the evergreen desert shrub known as creosote bush (Larrea divaricata, subspecies tridentata), which is found in the southwestern United States and Mexico. The leaves are ground into a powdered extract that can be brewed into tea, which was the form used by Native Americans for centuries to treat various conditions such as respiratory illness, chickenpox, snakebite and arthritis pain. More recently, chaparral has been prepared as a botanical in pill forms as well as in salves for topical application and concentrated extracts to be brewed into tea. Chaparral extracts have multiple active ingredients, the most prominent being nordihydroguaiaretic acid (NDGA), which has potent antioxidant properties. NDGA is found in many plant species and has been used as a food additive in low concentrations. As a botanical extract, chaparral has been claimed to have multiple beneficial effects as a free radical scavenger and useful for weight loss, liver wellness, cleansing of blood, improving immunity (cancer, HIV infection) and treating skin disorders. Chaparral is also claimed to retard aging and aid in wellbeing. However, chaparral preparations have not been shown to be effective in any medical condition.

Hepatotoxicity

Liver injury attributable to chaparral was first reported in 1990 and subsequently more than two dozen cases of clinically apparent liver injury attributed to chaparral have been published. The time to onset varied from 3 weeks to several years, but was usually within 3 to 12 weeks of starting daily ingestion or increasing the daily dose. The pattern of injury was typically hepatocellular with an acute viral hepatitis-like presentation and marked elevations in serum aminotransferase levels, but minimal increase in alkaline phosphatase. Autoimmune and immunoallergic features were uncommon. Several reported cases have been severe and some have led to emergency liver transplantation. Subclinical cases and serum enzyme elevations without symptoms may occur but have not been well characterized. Despite the several reports of liver injury caused by chaparral, over-the-counter products with chaparral are still available commercially and on the internet. For unclear reasons, there have been no cases of liver injury clearly implicating chaparral published since 2005.

Mechanism of Injury

Chaparral leaf extracts have many components but the most prominent is NDGA, an antioxidant which affects many intrahepatic pathways, including those involving cyclooxygenases and lipoxygenases. The rare cases of liver injury reported with chaparral use have had idiosyncratic features, and the rapid recurrence after reexposure and finding of eosinophils on liver biopsy suggest an allergic or immunological cause of injury. As with other reported herbal toxicities, the liver injury attributed to chaparral may have been due to contaminants or improperly prepared extracts.

Outcome and Management

Hepatotoxicity from chaparral is rare, but some cases have been severe leading to acute liver failure. Other instances have been reported to lead to cirrhosis, but cases of chronic hepatitis or vanishing bile duct syndrome have not been reported. Recurrence after reexposure has occurred.

Drug Class: Herbal and Dietary Supplements

CASE REPORT

Case 1. Severe acute hepatitis due to chaparral.

[Modified from: Katz M, Saibil F. Herbal hepatitis: subacute hepatic necrosis secondary to chaparral leaf. J Clin Gastroenterol 1990; 12: 203-6. PubMed Citation]

A 33 year old woman developed anorexia and nausea followed by jaundice 2 to 3 months after starting chaparral leaf (15 tablets per day) for a benign breast lump and general health on the advice of a friend. She decreased the number of tablets taken from 15 to 1 per day and her symptoms improved, but on increasing to 7 per day, she redeveloped nausea, jaundice, pale stools and increase in abdominal girth. Upon stopping chaparral leaf, her appetite returned but she continued to have fatigue and jaundice and sought medical advice. Her medical history was negative for liver disease, alcohol use or risk factors for viral hepatitis. Physical examination showed jaundice, ascites and peripheral edema without rash, fever or splenomegaly. Laboratory tests showed a total serum bilirubin of 12.0 mg/dL with marked elevations in serum aminotransferase levels (ALT 1385 U/L, AST 1285 U/L), with modest increases in alkaline phosphatase (285 U/L). Serum albumin was 2.8 g/dL and prothrombin time was 19 seconds. Tests for acute hepatitis A and B and Epstein Barr virus infection were negative as were autoantibodies. With stopping chaparral, she rapidly improved (Table) and after 3 weeks underwent liver biopsy, which showed severe hepatitis and submassive necrosis. She remained fatigued and had persistence of minor elevations in serum ALT for 12 months after stopping the botanical. In longterm follow-up, liver tests returned to normal.

Key Points

Medication:	Chaparral (1-15 tablets per day)
Pattern:	Hepatocellular (R=15.7)
Severity:	4+ (jaundice, hospitalization, prolonged prothrombin time)
Latency:	3 months
Recovery:	12 months
Other medications:	None mentioned

Laboratory Values

Time After Stopping	ALT (U/L)	Alk P (U/L)	Bilirubin (mg/dL)	Protime (seconds)	Other
1 week	1285	285	12.0	19	Admission
1.5 weeks	708		10.1	22	
1 month	317		3.5	15	Discharged
2 months	123	110	1.2	12.6	
3 months	80	130	1.2	11.9	
4 months	60	120	0.9	12.6	
12 months	32	32	1.0	12.0	Symptoms resolved
3 years	21	36	0.5	12.0	
Normal	**<40**	**<115**	**<1.2**	**<13**	

Comment

This initial case report of severe hepatitis attributed to chaparral use was published 7 years after its occurrence in 1983. A young woman developed a severe viral hepatitis-like syndrome 3 months after starting chaparral and had a temporary improvement on lowering the dose, and subsequent worsening with increasing it. Serum liver tests were not available from these periods of dose adjustment, but the clinical history suggested an association of disease severity with dosage and a positive rechallenge. When she presented to medical evaluation, she had evidence of severe hepatitis with jaundice and marked serum aminotransferase elevations along with ascites and prolongation of the prothrombin time. She began to improve between 1 and 2 weeks after stopping chaparral. A liver biopsy documented the severity of the liver injury (submassive necrosis with an estimated 60% loss of parenchyma). Symptoms and minor serum enzyme elevations persisted for at least 4 months after stopping, with full documentation of resolution when she was seen a year after stopping chaparral. The component of chaparral leaf extracts that is responsible for hepatotoxicity is not known; features of the disease suggest that the liver injury is idiosyncratic rather than a direct toxic effect.

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Chaparral – Generic

DRUG CLASS

Herbal and Dietary Supplements

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NUMBER	MOLECULAR FORMULA	STRUCTURE
Chaparral	84603-70-3	Herbal mixture	Not applicable

ANNOTATED BIBLIOGRAPHY

References updated: 23 January 2017

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; mentions that chaparral leaf has led to 10 reported cases of hepatocellular injury, including at least one case of acute liver failure).

Seeff L, Stickel F, Navarro VJ. Hepatotoxicity of herbs 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]*

describes results of the FDA analysis of cases of liver injury attributed to chaparral, which included cases of acute liver failure and others resulting in cirrhosis).

Katz M, Saibil F. Herbal hepatitis: subacute hepatic necrosis secondary to chaparral leaf. J Clin Gastroenterol 1990; 12: 203-6. PubMed PMID: 2324485.

(33 year old woman developed nausea followed by jaundice 3 months after starting chaparral, improving on lowering the dose and worsening on increasing [bilirubin 12.0 mg/dL, ALT 1385 U/L, protime 19 sec], with slow improvement on stopping, resolving in 12 months: Case 1).

Clark F, Dallas R, Reed R. From the Centers for Disease Control and Prevention. Chaparral-induced toxic hepatitis—California and Texas, 1992. MMWR 1992; 41: 812-4. PubMed PMID: 1406577.

(Two patients with severe hepatitis attributed to ingestion of chaparral; a 42 year old man and 41 year old woman who presented with jaundice 6 and 11 weeks after starting chaparral [bilirubin 16.6 and 30 mg/dL, AST 1077 and 3560 U/L, Alk P 133 and normal], resolving within 8 and 12 weeks of stopping).

Smith BC, Desmond PV. Acute hepatitis induced by ingestion of the herbal medication chaparral. Aust N Z J Med 1993; 23: 526. PubMed PMID: 8297290.

(36 year old woman developed jaundice and pruritus 8 weeks after starting chaparral [peak bilirubin 19.1 mg/dL, AST 674 U/L, Alk P 242 U/L], with resolution 4 months after stopping).

Alderman S, Kailas S, Goldfarb S, Singaram C, Malone DG. Cholestatic hepatitis after ingestion of chaparral leaf: confirmation by endoscopic retrograde cholangiopancreatography and liver biopsy. J Clin Gastroenterol 1994; 19: 242-7. PubMed PMID: 7806838.

(45 year old woman developed jaundice 2 months after starting chaparral for alcohol avoidance [bilirubin 11.6 rising to 35 mg/dL, ALT 1611 U/L, Alk P 265 U/L], with temporary worsening, prednisone therapy and eventual recovery over next 3 months).

Gordon DW, Rosenthal G, Hart J, Sirota R, Baker AL. Chaparral ingestion. The broadening spectrum of liver injury caused by herbal medications. JAMA 1995; 273: 489-90. PubMed PMID: 7837368.

(60 year old woman developed jaundice 10 months after starting chaparral [and 3 weeks after dose increase] with progressive liver failure [bilirubin 12.4 rising to 35.5 mg/dL, ALT 341 U/L, Alk P 186 U/L, protime 15.9 rising to 28 seconds], undergoing successful emergency liver transplantation).

Stashower ME, Torres RZ. Chaparral and liver toxicity. JAMA 1995; 274: 871; author reply 871-2. PubMed PMID: 7674494.

(Letter in response to Gordon [1995] pointing out that chaparral is not an herb, but a woody shrub).

Ippen H. Chaparral and liver toxicity. JAMA 1995; 274: 871; author reply 871-2. PubMed PMID: 7674493.

(Letter in response to Gordon [1995], questioning the actual plant being described, the term chaparral referring to several species and suggesting use of exact botanical names: Larrea divaricata, subsp tridentata).

Fleiss PM. Chaparral and liver toxicity. JAMA 1995; 274: 871; author reply 871-2. PubMed PMID: 7674492.

(Letter in response to Gordon [1995], questioning whether chaparral was the cause of the liver injury and not diltiazem [which was also being taken] or a contaminant of the botanical product).

Batchelor WB, Heathcote J, Wanless IR. Chaparral-induced hepatic injury. Am J Gastroenterol 1995; 90: 831-3. PubMed PMID: 7733101.

(Two patients; 71 year old man developed jaundice and ascites 2 months after starting daily chaparral intake [bilirubin 17.8 mg/dL, AST 385 U/L, Alk P 149 U/L], resolving within 2 months of stopping and recurring 1 month after restarting [bilirubin 9.9 mg/dL, AST 767 U/L, Alk P 304 U/L]; 43 year old woman developed nausea and then jaundice 6 weeks after starting chaparral for headaches [bilirubin 9.7 mg/dL, AST 1612 U/L, Alk P 129 U/L], resolving within 4 months of stopping).

Sheikh NM, Philen RM, Love LA. Chaparral-associated hepatotoxicity. Arch Intern Med 1997; 157: 913-9. PubMed PMID: 9129552.

(Summary of 13 reports of hepatotoxicity reported to the FDA between 1992-4: 11 women and 2 men, ages 25 to 60 years, taking 8 different chaparral preparations [mostly single product capsules], for 3 to 12 weeks in most, but for 1 to many years in some, for various indications [weight loss, acne, allergies, blood thinning, cleanser, arthritis and asthma], typically presenting with jaundice and marked ALT and AST elevations but minor increases in Alk P, resolving in most but 2 required liver transplant and 4 developed cirrhosis).

Shad JA, Chinn CG, Brann OS. Acute hepatitis after ingestion of herbs. South Med J 1999; 92: 1095-7. PubMed PMID: 10586838.

(Two cases; 33 year old woman developed ALT elevations [488 U/L] within 8 weeks of starting "bee pollen", resolving within 6 weeks of stopping; 69 year old man developed jaundice 6 weeks after starting herbal mixture, including chaparral and bee pollen [bilirubin 27.2 mg/dL, ALT 1081 U/L, Alk P 272 U/L], resolving within 8 weeks of stopping).

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 chaparral although the usual presentation is as an acute hepatitis-like syndrome rather than cholestasis).

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

(Review and description of patterns of liver injury due to herbals, including discussion of potential risk factors, and herb-drug interactions; chaparral is listed and discussed as potential cause of acute liver failure and cirrhosis; the specific hepatotoxic compound in chaparral extracts is unknown).

Haller CA, Dyer JE, Ko R, Olson KR. Making a diagnosis of herbal-related toxic hepatitis. West J Med 2002; 176; 39-44. PubMed PMID: 11788538.

(Two cases demonstrating the difficulties of identifying the toxic component of herbals; 42 year old woman developed fatigue 10 weeks after starting 3 herbal medications [bilirubin 1.2 mg/dL, ALT 3386 U/L, Alk P 100 U/L], ultimately attributed to Jin Bu Huan; 39 year old woman developed acute liver failure after taking multiple herbals [bilirubin 42.7 mg/dL, ALT 349 U/L, INR 3.9] believed to be due to chaparral).

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; discusses chaparral as a potential cause of acute liver failure and cirrhosis).

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 at two US medical centers during 2001-2, 10 were potentially caused by herbals; 1 was attributed to chaparral).

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 3 cases due to chaparral).

Kauma H, Koskela R, Mäkisalo H, Autio-Harmainen H, Lehtola J, Höckerstedt K. Toxic acute hepatitis and hepatic fibrosis after consumption of chaparral tablets. Scand J Gastroenterol 2004; 39: 1168-71. PubMed PMID: 15545179.

(22 year old woman developed pruritus and jaundice 8 weeks after starting chaparral [2 tablets daily] [bilirubin 11.8 mg/dL, ALT 2871 U/L, Alk P511 U/L], with rapid improvement on stopping, but recurrence within 2 weeks of restarting [bilirubin 8.8 mg/dL, ALT 1084 U/L, Alk P 379 U/L], resolving within 2 months of finally stopping).

Pak E, Esrason KT, Wu VH. Hepatotoxicity of herbal remedies: an emerging dilemma. Prog Transplant 2004; 15: 91-6. PubMed PMID: 15264453.

(Review of hepatotoxicity of herbal medications stressing the recent rise in numbers of cases; summarizing a single case report and FDA summary of chaparral hepatotoxicity).

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

(Review of herbals as a cause of hepatotoxicity, with specific discussion of chaparral as a cause of acute hepatitis, acute liver failure and cirrhosis).

García-Cortés M, Borraz Y, Lucena MI, Peláez G, Salmerón J, Diago M, Martínez-Sierra MC, et al. [Liver injury induced by "natural remedies": an analysis of cases submitted to the Spanish Liver Toxicity Registry]. Rev Esp Enferm Dig 2008; 100: 688-95. Spanish. PubMed PMID: 19159172.

(Among 521 cases of drug induced liver injury submitted to Spanish registry, 13 [2%] were due to herbals, none due to chaparral).

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, none due to chaparral).

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; chaparral has been linked to hepatotoxicity by a series of case reports).

Stickel F, Schuppan D. Herbal medicine in the treatment of liver diseases. Dig Liver Dis 2007; 39: 293-304. PubMed PMID: 17331820.

(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).

Teschke R, Wolff A, Frenzel C, Schulze J, Eickhoff A. Herbal hepatotoxicity: a tabular compilation of reported cases. Liver Int 2012; 32: 1543-56. *(Systematic* PubMed PMID: 22928722.

tabulation of the literature on hepatotoxicity of herbals and lists five publications on chapparal).

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

(Review of HDS associated hepatotoxicity with discussion of chaparral which was used in the form of teas, capsules, tablets and salves and perceived to have antimicrobial and antioxidant activities, but subsequently associated with more than a dozen cases of liver injury including two requiring liver transplantation and 4 resulting in cirrhosis).

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%], and that these other diagnoses weakened the causality assessment in most instances).

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, but none were attributed to a Move Free product or Chinese skullcap).

Licata A, Macaluso FS, Craxì A. Herbal hepatotoxicity: a hidden epidemic. Intern Emerg Med 2013; 8: 13-22. PubMed PMID: 22477279.

(Review and commentary on herbal hepatotoxicity discusses Larrea tridentata as being linked to at least 13 cases of liver injury with different clinical patterns including acute liver failure and chronic injury resulting in cirrhosis).

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 HDS induced liver injury including regulatory problems, difficulties in diagnosis and causality assessment; mentions that chaparral has been linked to cases of liver injury some of which were severe enough to require liver transplantation).

Navarro VJ, Barnhart H, Bonkovsky HL, Davern T, Fontana RJ, Grant L, Reddy KR, et al. Liver injury from herbals and dietary supplements in the U.S. Drug-Induced Liver Injury Network. Hepatology 2014; 60:1399-408. PubMed PMID: 25043597.

(Among 85 cases of HDS associated liver injury [not due to anabolic steroids] enrolled in a US prospective study between 2004 and 2013, none were attributed to a chaparral containing product).

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

(Review of HDS induced liver injury including regulatory problems, difficulties in diagnosis and causality assessment, mentions that chaparral has been associated with severe liver injury and liver failure).

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. PubMed PMID: 25500423.

(Extensive review of possible beneficial as well as harmful effects of herbal products on the liver mentions that there have been numerous reports of liver injury from chaparral ranging from elevated enzyme levels alone to fulminant hepatitis).

Stickel F, Shouval D. Hepatotoxicity of herbal and dietary supplements: an update. Arch Toxicol. 2015; 89: 851-65. PubMed PMID: 25680499.

(Extensive review of liver injury due to HDS mentions that Herbalife has been implicated in 54 cases of liver injury, 7 with a positive rechallenge, but that the cause of the injury remains unknown and that few cases have been published since 2011; does not mention Move Free products).

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: 1340-52. PubMed PMID: 25754159.

(Among 899 cases of drug induced liver injury enrolled in a prospective database between 2004 and 2012, HDS were implicated in 145 [16%], none of which were primarily attributed to chaparral: see Navarro [2014]).