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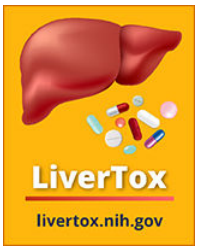

Spirulina

Updated: April 10, 2019.

OVERVIEW

Introduction

Spirulina is a dietary supplement made from blue-green algae (cyanobacteria: Arthrospira platensis) that is used both as a food and as a medicinal supplement to counteract unintentional weight loss and to ameliorate a variety of medical conditions including attention-deficit hyperactivity disorder, allergic rhinitis, hypertension, diabetes, stress, fatigue, anxiety and depression. Spirulina has been implicated in isolated case reports in causing clinically apparent liver injury, but the role of spirulina as opposed to other herbal components or contaminants has not been shown. Liver injury due to spirulina must be very rare if it occurs at all.

Background

Spirulina is a dietary supplement prepared from the biomass of blue-green algae which is rich in protein, vitamins and minerals. Spirulina refers to a large number of photosynthetic eubacterial species belonging to the phylum Cyanobacteria (Arthrospira platensis and maxima). While known as blue-green algae, spirulina it is a prokaryotic, eubacterial species belonging to the phylum Cyanobacteria. Spirulina typically grows in warm open lakes with high alkalinity and can be contaminated with other blue-green algae that produce toxins (microcystins). Spirulina has been used as a food and source of nutrients for centuries by the people of Mexico and Central America but only recently has been prepared as commercial dietary supplements. Spirulina is particularly rich in protein (65% to 70%) as well as vitamins, phycocyanin, beta-carotene, polyunsaturated fatty acids, linolenic acid, calcium and iron. The blue-green pigment phycocyanin accounts for up to 20% of its dry weight and has been proposed to be the active ingredient responsible for its medicinal properties. In animal experiments, spirulina has demonstrated antioxidant, antiinflammatory and analgesic effects and has been well tolerated without evidence of toxicity even in high doses. There have been limited studies in humans, but it has not been proven to be effective in treating any medical condition. Studies have found it to be safe without significant adverse events.

Hepatotoxicity

In controlled trials, spirulina has not been linked to serum enzyme elevations or to instances of clinically apparent liver injury. Indeed, in several studies serum aminotransferase levels have decreased with spirulina therapy, and it has been evaluated in uncontrolled studies as a potential therapy of nonalcoholic steatohepatitis. Despite its long history of use and safety, spirulina has recently been implicated in at least published case of clinically apparent liver injury and in several reports of hepatic injury to national registries of adverse drug events. In the single case report, the latency to onset of jaundice was 5 weeks and the injury was hepatocellular, without immunoallergic or autoimmune features and with rapid and complete recovery on withdrawal. The

patient was also taking several other drugs that can cause liver injury which were stopped at the same time including acarbose and simvastatin. Thus, spirulina may cause clinically apparent liver injury, but it is quite rare.

Likelihood score: D (possible rare cause of clinically apparent liver injury).

Mechanism of Injury

The mechanism by which spirulina might cause liver injury is unclear. Contamination of the product with other cyanobacteria with cytotoxic microcystins is a possible explanation. The concentration, purity and freedom from contaminants from the commercial preparations of spirulina implicated in liver injury have not been reported.

Outcome and Management

The severity of the liver injury in reports of spirulina hepatotoxicity has varied from mild, asymptomatic elevations in serum enzymes to self-limiting, clinically apparent hepatitis. There have been no reports of acute liver failure, chronic hepatitis or vanishing bile duct syndrome attributed to spirulina. There is no information on management or the role for corticosteroids or other interventions except for prompt discontinuation of the suspected agent.

Drug Class: Herbal and Dietary Supplements

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Spirulina – Generic

DRUG CLASS

Herbal and Dietary Supplements

SUMMARY INFORMATION

Fact Sheet at MedlinePlus, NLM

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NUMBER	MOLECULAR FORMULA	STRUCTURE
Spirulina	S058500000	Extract	Not applicable

ANNOTATED BIBLIOGRAPHY

References updated: 10 April 2019

Abbreviations used: HDS, herbal and dietary supplements

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; spirulina is not discussed).

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 HDS; spirulina is not discussed).

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

(Comprehensive review of herbal associated hepatotoxicity; spirulina is not listed as causing hepatotoxicity).

Iwasa M, Yamamoto M, Tanaka Y, Kaito M, Adachi Y. Spirulina-associated hepatotoxicity. Am J Gastroenterol. 2002;97:3212–3. PubMed PMID: 12492223.

(52 year old Japanese man with hypertension and diabetes developed liver test abnormalities 2 weeks after starting spirulina [ALT 136 U/L] which worsened on continuing [bilirubin 2.2 mg/dL, ALT 1726 U/L, Alk P 281 U/L, GGT 301 U/L], resolving within 6 weeks of stopping spirulina as well as his other medications including simvastatin, amlodipine and acarbose).

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, none were attributed to spirulina).

Ferreira-Hermosillo A, Torres-Duran PV, Juarez-Oropeza MA. Hepatoprotective effects of Spirulina maxima in patients with non-alcoholic fatty liver disease: a case series. J Med Case Rep. 2010;4:103. PubMed PMID: 20370930.

(Three patients with nonalcoholic fatty liver disease were treated with spirulina [4.5 g daily] and had improvements in serum ALT, triglyceride and LDL-cholesterol levels without adverse side effects).

Deng R, Chow TJ. Hypolipidemic, antioxidant, and antiinflammatory activities of microalgae Spirulina. Cardiovasc Ther. 2010;28:e33–45. PubMed PMID: 20633020.

(Review of the preclinical studies of spirulina suggesting hypolipidemic, antioxidant and antiinflammatory activity and the few clinical studies concludes that despite isolated reports of toxicity, "Spirulina is generally considered safe for human consumption supported by its long history of use as food source, and its favorable safety profile in animal studies").

Marles RJ, Barrett ML, Barnes J, Chavez ML, Gardiner P, Ko R, Mahady GB, et al. United States pharmacopeia safety evaluation of spirulina. Crit Rev Food Sci Nutr. 2011;51:593–604. PubMed PMID: 21793723.

(Formal systematic analysis of the safety of spirulina by the US Pharmacopeia based upon the published literature as well as FDA and other national adverse event registries identified multiple reports of possible liver injury; one published [Iwasa 2002], 5 from the FDA's MedWatch and 3 from a Canadian registry, but none from Australia, the UK or Europe; because the reports had inadequate detail to exclude competing diagnoses and possible contaminants, the USP concluded that spirulina should be considered safe, but that prospective studies of its safety were warranted).

Karkos PD, Leong SC, Karkos CD, Sivaji N, Assimakopoulos DA. Spirulina in clinical practice: evidence-based human applications. Evid Based Complement Alternat Med. 2011;2011:531053. PubMed PMID: 18955364.

(Review of the potential clinical benefits of spirulina concludes that "what the literature suggests is that Spirulina is a safe food supplement without significant side effects but its role as a drug remains to be seen").

Yakoot M, Salem A. Spirulina platensis versus silymarin in the treatment of chronic hepatitis C virus infection. A pilot randomized, comparative clinical trial. BMC Gastroenterol. 2012;12:32. PubMed PMID: 22497849.

(Among 66 patients with chronic hepatitis C treated with spirulina or silymarin for 6 months, serum ALT levels decreased more with spirulina [-24 vs –7 U/L] and serum HCV RNA levels decreased in some patients, and there were no serious adverse events).

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 and supplements; does not list spirulina).

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 mention spirulina).

Mazokopakis EE, Papadomanolaki MG, Fousteris AA, Kotsiris DA, Lampadakis IM, Ganotakis ES. The hepatoprotective and hypolipidemic effects of Spirulina (Arthrospira platensis) supplementation in a Cretan population with non-alcoholic fatty liver disease: a prospective pilot study. Ann Gastroenterol. 2014;27:387–94. PubMed PMID: 25331487.

(Among 15 men from Crete with nonalcoholic fatty liver disease treated with spirulina [6 g daily] for 6 months, mean ALT levels decreased [104 to 65 U/L] as did AST [66 to 41 U/L], cholesterol [275 to 250 mg/dL] and body weight [103 to 95 kg], and no patient reported any side effects).

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 spirulina).

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 does not mention or discuss spirulina).

Jensen GS, Drapeau C, Lenninger M, Benson KF. Clinical safety of a high dose of phycocyanin-enriched aqueous extract from Arthrospira (Spirulina) platensis: results from a randomized, double-blind, placebo-controlled study with a focus on anticoagulant activity and platelet activation. J Med Food. 2016;19:645–53. PubMed PMID: 27362442.

(Among 24 adults with chronic joint pain treated with high doses of an aqueous spirulina extract or placebo for 2 weeks, pain scores and serum ALT and AST levels improved with the extract vs placebo, while other laboratory values, platelet numbers and coagulation measurements did not change).

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 does not mention or discuss spirulina).

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; does not mention spirulina).

Zeinalian R, Farhangi MA, Shariat A, Saghafi-Asl M. The effects of Spirulina Platensis on anthropometric indices, appetite, lipid profile and serum vascular endothelial growth factor (VEGF) in obese individuals: a

randomized double blinded placebo-controlled trial. BMC Complement Altern Med. 2017;17:225. PubMed PMID: 28431534.

(Among 64 obese adults treated with spirulina [500 mg] or placebo twice daily for 12 weeks, weight decreased slightly more with spirulina [-1.6 vs -0.6 kg] while change in serum lipids did not differ in the two groups, and "no side effects of treatment were observed").

Finamore A, Palmery M, Bensehaila S, Peluso I. Antioxidant, immunomodulating, and microbial-modulating activities of the sustainable and ecofriendly spirulina. Oxid Med Cell Longev. 2017;2017:3247528. PubMed PMID: 28182098.

(Review of the preclinical and clinical evidence for antioxidant, antiinflammatory and immunomodulatory effects of spirulina, mentions that that expert committees have concluded that it is generally safe and is not a serious risk to health).