

## Severe Hepatotoxicity Due to Hydroxycut: A Case Report

Michael Shim · Sammy Saab

Received: 13 April 2008 / Accepted: 15 May 2008 / Published online: 26 July 2008  
© Springer Science+Business Media, LLC 2008

### Case

A 28-year-old male was transferred to our institution with 3 weeks of fatigue, dyspnea on exertion, jaundice, and dark urine. In an effort to lose weight, he had been taking Hydroxycut, two tablets, two to three times per day (which is within the manufacturer's suggested dosing), from 3 months prior to admission up until the development of symptoms. Additionally, for soreness associated with his aerobic exercise program, he took an over-the-counter pain-reliever containing acetaminophen 250 mg, aspirin 250 mg, and caffeine 65 mg, four tablets per day for the 10 days leading up to the development of his symptoms. He was not a heavy drinker of ethanol, drinking 2–3 beers per week. Physical examination was unremarkable and without stigmata of chronic liver disease. Laboratory analysis revealed a serum aspartate aminotransferase of 1049 U/l (normal range 7–36 U/l), alanine aminotransferase of 2272 (normal 4–45 U/l), alkaline phosphatase of 152 U/l (normal

31–103 U/l), total bilirubin of 18.1 mg/dl (normal 0.2–1.1 mg/dl), conjugated bilirubin of 9.0 (normal 0.0–0.2 mg/dl), albumin level of 4 g/dl (normal 3.7–5.1 g/dl), prothrombin time of 12.8 s (normal 9.2–10.6 s), normal complete blood count, normal electrolyte panel, and normal estimated glomerular filtration rate. Aminotransferase levels and prothrombin time began to decline immediately after admission and bilirubin peaked on hospital day 2 at 22.4 mg/dl. Acetaminophen level was undetectable. Tests for viral hepatitis were negative. Ferritin was markedly elevated at 9519 ng/ml (normal 10–210 ng/ml). HFE genotyping was negative for H63D or C282Y mutations. Antinuclear antibody titer was 1:40 (normal, <1:40), smooth muscle antibody titer was 1:20 (normal, <1:20), liver kidney microsomal antibody was negative, and soluble liver antigen antibody was negative. Serum copper level was 96 mcg/dl (normal 70–140 mcg/dl) and ceruloplasmin was 31 mg/dl (normal 18–54 mg/dl). Twenty-four hour urine copper level was 290 mcg/dl (normal 3–50 mcg/dl). Slit-lamp examination for Kaiser-Fleischer rings was equivocal. Abdominal ultrasound with Doppler and computed tomography (CT) scan with intravenous contrast were both normal. The patient's liver function tests continued to improve and he was discharged on hospital day 9.

---

Recent reports have identified an association between hepatotoxicity and the weight loss supplement *Hydroxycut* (MuscleTech, Mississauga, Ontario, Canada). Here we report a case of severe hepatotoxicity associated with *Hydroxycut* and summarize the published data identifying an association between the herbal compounds in *Hydroxycut* and hepatotoxicity.

---

M. Shim (✉)  
Division of Digestive Diseases, David Geffen School  
of Medicine at UCLA, 1629 Veteran Avenue, Apt. 5,  
Los Angeles, CA 90024, USA  
e-mail: shimm01@ucla.edu

S. Saab  
UCLA Department of Medicine, Division of Digestive Diseases,  
Box 957302, 200 Medical Plaza Suite 214, Los Angeles,  
CA 90095-7302, USA

### Discussion

Though the markedly elevated 24-h urine copper level and slit-lamp examination equivocal for Kaiser-Fleischer rings suggested the possibility of underlying Wilson disease, the normal serum copper and ceruloplasmin levels, lack of underlying cirrhosis, lack of supportive family history, lack of concomitant neurological or psychiatric disturbance, and lack of hemolysis all argued against this diagnosis. In the end, it was felt that the patient's elevated urinary copper

level was due to his marked cholestasis and that his presentation was most consistent with hepatotoxicity associated with *Hydroxycut*.

This is the third reported case of hepatotoxicity associated with *Hydroxycut*. The first case demonstrated a predominantly hepatocellular injury pattern on liver function tests with peak alanine aminotransferase 3962 U/l that resolved after 4 weeks, while the other demonstrated a predominantly cholestatic pattern of injury (confirmed on liver biopsy) that resolved after 2 months [1]. In both cases, the patients were taking three tablets three times per day.

The manufacturer's list of active ingredients in *Hydroxycut* is shown in Table 1 [2]. Of the ingredients listed, extracts of *Garcinia cambogia*, *Gymnema sylvestre*, and green tea (*Camellia sinensis*) have been associated with cases of severe hepatotoxicity. In the one case associated with *Garcinia cambogia* and *Gymnema sylvestre*, the patient had taken a 7-day course of two dietary weight-loss supplements, one of which contained both *Garcinia cambogia* and *Gymnema sylvestre*, the week prior to becoming jaundiced [3]. This particular case progressed to fulminant hepatic failure and death. The authors speculated that a synergistic interaction between the weight-loss supplements and chronic use of a leukotriene antagonist inhibitor, a class of medicine that has been associated with severe hepatotoxicity, resulted in her fulminant and ultimately fatal presentation.

There have been at least 11 case reports associating green tea extract (*Camellia sinensis* extract) with severe hepatotoxicity [4–13]. In all cases, except two which required liver transplantation [9, 13], there was eventual recovery after cessation of the supplement containing the extract. In one case [4], there was some suggestion of causation, as the patient rechallenged herself with the same supplement and again presented with severe hepatotoxicity.

The mechanism of the potential toxicity of green tea extract is unclear. There has been speculation that the

predominant polyphenol or catechin within this extract, epigallocatechin-2-gallate (EGCG), may be the causative agent [13]. An in vitro study suggested that high concentrations of EGCG were cytotoxic to rat liver cells [14]. However, this manuscript concluded that the oral bioavailability of EGCG in green tea extracts was probably too low to produce serum levels approaching the levels that were cytotoxic to the rat liver cells. Because of this, it has been further proposed that the hepatotoxicity associated with green tea extract may be an idiosyncratic and/or hypersensitivity-type reaction or that an undetected compound contaminating the extract may be the causative agent [4, 13, 14].

Finally, we cannot rule out an interaction between the compounds in *Hydroxycut* and the acetaminophen the patient was taking concomitantly. Although we found no studies directly investigating this possibility, one might speculate that one or more of the compounds in *Hydroxycut* could induce or stimulate the CYP2E1 cytochrome system, lead to more production of *N*-acetyl-*p*-benzo-quinone imine (NAPQI), and thus accentuate acetaminophen-induced hepatotoxicity, much like chronic ethanol consumption.

Caution should be exercised by consumers using the weight-loss supplement *Hydroxycut*. There is evidence that extracts of *Garcinia cambogia*, *Gymnema sylvestre*, and green tea (*Camellia sinensis*) contained in *Hydroxycut* may be associated with severe and even fatal hepatotoxicity.

## References

1. Stevens T, Qadri A, Zin NN (2005) Two patients with acute liver injury associated with use of the herbal weight-loss supplement Hydroxycut. *Ann Intern Med* 142(6):477–478
2. [http://www.hydroxycut.com/PRODUCT\\_POPUP/HYD\\_supplement\\_facts.html](http://www.hydroxycut.com/PRODUCT_POPUP/HYD_supplement_facts.html)
3. Actis GC, Bugianesi E, Ottobrelli A, Rizzetto M (2007) Fatal liver failure following food supplements during chronic treatment with montelukast. *Dig Liver Dis* 39(10):953–955. doi: 10.1016/j.dld.2006.10.002
4. Bonkovsky HL (2005) Hepatotoxicity associated with supplements containing Chinese green tea (*Camellia sinensis*). *Ann Intern Med* 144(1):68–71
5. Porcel JM, Bielsa S, Madronero AB (2005) Hepatotoxicity associated with green tea extracts [electronic letter]. Accessed at <http://www.annals.org> on 3 June 2005
6. Garcia-Moran S, Saez-Royuela F, Gento E, Lopez Morante A, Arias L (2004) Acute hepatitis associated with *Camellia thea* and *Orthosiphon stamineus* ingestion. *Gastroenterol Hepatol* 27:559–560. doi:10.1157/13068145
7. Thiolet C, Menecier D, Bredin C, Moulin O, Rimlinger H, Nizou C et al (2002) Acute cytolysis induced by Chinese tea. *Gastroenterol Clin Biol* 26:939–940
8. Vial T, Bernard G, Lewden B, Dumortier J, Descotes J (2003) Acute hepatitis due to exolise, a *Camellia sinensis*-derived drug. *Gastroenterol Clin Biol* 27:1166–1167
9. Gloro R, Hourmand-Ollivier I, Mosquet B, Mosquet L, Rousselot P, Salamé E et al (2005) Fulminant hepatitis during self-medication with hydroalcoholic extract of green tea. *Eur J Gastroenterol*

**Table 1** Listed ingredients in *Hydroxycut*

<i>Garcinia cambogia</i> extract
<i>Gymnema sylvestre</i> extract
Soy phospholipids
<i>Rhodiola rosea</i> extract
<i>Withania somnifera</i> extract
Green tea extract (as <i>Camellia sinensis</i> )
Caffeine anhydrous
White tea extract (as <i>Camellia sinensis</i> )
Oolong tea extract (as <i>Camellia sinensis</i> )
Other ingredients: hydroxypropyl cellulose, microcrystalline cellulose, polyvinylpyrrolidone, croscarmellose sodium, vegetable stearine, magnesium stearate, coating, silica, acesulfamepotassium, maltodextrin, propylene oxide

- Hepatol 17(10):1135–1137. doi:[10.1097/00042737-200510000-00021](https://doi.org/10.1097/00042737-200510000-00021)
10. Abu el Wafa Y, Benavente Fernández A, Talavera Fabuel A, Pérez Ramos MA, Ramos-Clemente JI (2005) Acute hepatitis induced by *Camellia sinensis* (green tea). Med Intern 22(6):298
  11. Dueñas Sadornil C, Fabregas Puigtió S, Duráñez R (2005) Hepatotoxicity due to *Camelia sinensis*. Med Clin (Barc) 122(17):677–678. doi:[10.1157/13061393](https://doi.org/10.1157/13061393)
  12. Pedros C, Cereza G, García N, Laporte JR (2003) Liver toxicity of *Camellia sinensis* dried etanolic extract. Med Clin (Barc) 121:598–599. doi:[10.1157/13053801](https://doi.org/10.1157/13053801)
  13. Molinari M, Watt KD, Kruszyna T, Nelson R, Walsh M, Huang WY et al (2006) Acute liver failure induced by green tea extracts: case report and review of the literature. Liver Transpl 12:1892–1895. doi:[10.1002/lt.21021](https://doi.org/10.1002/lt.21021)
  14. Schmidt M, Schmitz HJ, Baumgart A, Guédon D, Netsch MI, Kreuter MH et al (2005) Toxicity of green tea extracts and their constituents in rat hepatocytes in primary culture. Food Chem Toxicol 43:307–314. doi:[10.1016/j.fct.2004.11.001](https://doi.org/10.1016/j.fct.2004.11.001)