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LETTERS TO THE EDITOR

Hepatoxicity associated with weight-loss supplements: A case for better post-marketing surveillance

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Abstract

There is a growing number of case reports of hepatoxicity from the widely marketed weight-loss supplement Hydroxycut, which contains the botanical ingredient *Garcinia cambogia*. These case reports may substantially undercount the true magnitude of harm. Based on the past experience with harmful dietary supplements, US regulators should assume the more precautionary approach favored by Canada and Europe. Lacking effective adverse event surveillance for supplements, or the requirements to prove safety prior to coming to the market, case reports such as those summarized here assume added importance.

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Key words: Hydroxycut; Dietary supplements; Garcinia cambogia; Liver failure; Weight loss; Super citrimax; Hca-sx

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TO THE EDITOR

Dara *et al*[1] report on a case series of two patients with hepatotoxicity associated with the weight-loss supplement Hydroxycut, so named because it contains potentially hepatoxic hydroxycitric acid derived from the tropical fruit *Garcinia cambogia*[1]. Two earlier case reports in 2005 were also referenced[2]. To this count should be added two additional case reports of hepatoxicity associated with Hydroxycut[3,4]. An estimated 15% of the US population uses dietary supplements for weight loss[5], and Hydroxycut is the top selling product in this class and market, with roughly a million units sold per year[6]. With such wide usage, these six cases may underestimate the true incidence of hepatoxicity by several degrees of magnitude.

Each case report has similarities both in reported liver screening abnormalities and symptoms reported by patients, all of whom were otherwise healthy and experienced normalized hepatic function once they stopped taking the supplement. Table 1 synthesizes key laboratory findings and reported symptoms.

Poor regulation of dietary supplements in the US has been noted by consumer advocates, researchers and policymakers[7-10]. US manufacturers of dietary supplements are not required to conduct trials establishing safety or efficacy prior to marketing; only provide a copy of their label for the Food and Drug Administration (FDA) to review[7,9,11]. Ingredients do not need to be considered "generally regarded as safe" as pharmaceuticals or food additives do, and the FDA must prove that a supplement is harmful before taking regulatory action[9,11]. This means consumers in effect become unwitting subjects in a large scale post-marketing trial of a product's safety. Unfortunately, the FDA does a generally poor job of post-marketing monitoring of adverse events from supplements, only receiving reports of an estimated 1% of such events[11]. A recent search of FDA's adverse events surveillance database for "Hydroxycut", "hydroxycitric acid", "*Garcinia cambogia*", or "SuperCitrimax" (the proprietary blend of *Garcinia cambogia* used in Hydroxycut) yielded no reports[12]. Furthermore, the nation's poison control centers, which receive far more supplement adverse event reports than the FDA, lack the necessary coordination to act in a surveillance role[11]. Supplement manufacturers may not be forthcoming with information about emerging health risks from their products. The makers of the weight-loss supplement Metabolife 356, for example, withheld over 14 000 reports they had received over 5 years documenting serious adverse events associated with

Table 1 Patients, symptoms and laboratory values reported with hydroxycut associated hepatoxicity

Citation	Dara *et al*[1]		Jones *et al*[4]	Shim *et al*[3]	Stevens *et al*[2]	
Patient age (yr)	40	33	19	28	27	30
Patient gender	F	F	M	M	M	M
Reported symptoms/ duration	Fatigue, nausea, vomiting, cramping, fever, chills, anorexia/3 d	Fatigue, nausea, cramping, abdominal pain/2 wk	Nausea, vomiting, jaundice/6 d	Fatigue, dyspnea on exertion, jaundice/ 3 wk	Fatigue, jaundice/8 d	Fatigue, vomiting, jaundice, fever/10 d
Aspartate aminotransferase (U/L)	1020	934	1981	1049	1808	59
Alanine aminotransferase (U/L)	1150	570	1143	2272	3131	45
Serum alkaline phosphatase (U/L)	299	112	153	153	171	530
Serum bilirubin (mg/L)	6.7	209	117	181	78	78
Serum direct bilirubin (mg/L)	Not reported	142	68	90	Not reported	Not reported
Prothrombin time (s)	Not reported	Not reported	17.1	12.8	16	15

their ephedra-containing product, including myocardial infarction, stroke, seizure and death[7]. (Though not legally mandated to report serious adverse events until 2007[9,11], failure to act on such reports suggests an ethical lapse.) To be fair, the FDA has taken action to protect the public health from dangerous supplements, banning ephedra in 2004 due to its cardiac risk[13]. Formerly a common ingredient in numerous weight-loss supplements, ephedra was banned only after 155 deaths were associated with its use[14]. In contrast, regulators in Canada, the UK and Europe appear to take a more precautionary approach. The supplement kava-kava was banned in Canada in 2002 after 29 cases of hepatoxicity were associated with its use[15], and in the UK and Europe the following year after some 40 more cases were reported[16]. In the US, the FDA has issued a consumer advisory about possible hepatoxicity associated with kava-kava use, but has not banned the substance[17].

Faced with the aforementioned difficulties ensuring the safety of widely used dietary supplements, reliable and transparent case reports such as those cited above assume added importance. They may also underscore the need for US regulators to adopt the more precautionary post-marketing practices of their European and Canadian counterparts. Authorities should also exercise their responsibilities to the public's health by being empowered to practise more stringent and evidenced-based regulation of these products, many of whom could be considered pharmaceuticals due to their clear pharmacological effects and potent risks[9].

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