Dietary Supplements:
State & Industry Efforts to Enhance Transparency

(Industry Perspective)

Jen Johansen, VP of Quality, Regulatory & Government Affairs
Cyanotech Corporation/Nutrex Hawaii
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Hepatotoxicity associated with the dietary supplement OxyELITE Pro™ — Hawaii, 2013

David L. Johnston, Arthur Chang, Melissa Viray, Kevin Chatham-Stephens, Hua He, Ethel Taylor, Linda L. Wong, Joshua Schier, Colleen Martin, Daniel Fabricant, Monique Salter, Lauren Lewis and Sarah Y. Park

Dietary supplements are increasingly marketed to and consumed by the American public for a variety of purported health benefits. On 9 September 2012, the Hawaii Department of Health (HDOH) was notified of a cluster of acute hepatitis and fulminant hepatic failure among individuals with exposure to the dietary supplement OxyELITE Pro™ (OEP). HDOH conducted an outbreak investigation in collaboration with federal partners. Physicians were asked to report cases, defined as individuals with acute and fulminating hepatitis of unknown etiology on or after 1 April 2013, a history of weight-loss/muscle-building dietary supplement use during the 90 days before illness onset, and residence in Hawaii during the period of exposure. Reported cases’ medical records were reviewed, questionnaires were administered, and a product investigation, including chemical analysis and traceback, was conducted. Of 76 reports, 44 (58%) met case definition of there, 36 (82%) reported OEP exposure during the two months before illness onset. No other common supplements or exposures were observed. Within the OEP-exposed subset, two patients required liver transplantation, and a third patient died. Excessive product dosing was not reported. No unique lot numbers were identified. There were multiple mainland distribution points, and lot numbers common to cases in Hawaii were not identified in continental states. Product analysis found contained ingredients consistent with labeled ingredients; the mechanism of hepatotoxicity was not identified. We report one of the largest statewide outbreaks of dietary supplement-associated hepatotoxicity. The implicated product was OEP. The increasing popularity of dietary supplements raises the potential for additional clusters of diet-supplement-related adverse events.

Keywords: toxin, hepatitis, dietary supplements

Introduction

More than half of adults in the United States use dietary supplements, most commonly to improve or maintain overall health. Weight-loss supplements are especially popular. Although dietary supplements often appear in a capsule or tablet similar to prescription medicine, they are regulated as food and are not subject to the same premarket requirements for safety or efficacy; thus, post-market surveillance and epidemiology are the only means of identifying problems in the marketplace and protect consumers. Over 1100 agents, including drugs and herbs, are recognized to cause liver injury. However, attributing causality is often challenging given the limited clinical laboratory tests to identify specific hepatotoxins. Hepatotoxicity has been previously reported as a serious adverse reaction to dietary supplement consumption; a study of 20 cases of fulminant hepatic failure seen by a liver transplantation service found half of the cases were active or recent users of dietary supplements with known potentially hepatotoxic supplements or herbs, with 7 cases having no other etiology identified. A review of the United Network for Organ Sharing liver transplant database from 1990 to 2002 demonstrated an herbal etiology in 3% of 270 patients. Here we report a cluster of acute hepatitis and fulminant hepatic failure associated with the dietary supplement OxyELITE Pro™.

Acknowledgments

Correspondence to David L. Johnston, MRCP (750 Punchbowl St. Suite 101, Honolulu, HI 96813, USA; Email: david.johnston@hawaii.gov)

a. Disease Outbreak Control Division, Hawaii Department of Health, USA
b. Health Outbreak Branch, National Center for Environmental Health, Division of Control and Prevention, Atlanta, GA, USA
c. The Queen’s Medical Center, Honolulu, HI, USA
d. National Products Association, Washington, DC, USA

Nutrex Hawaii | www.nutrex-hawaii.com
Who We Are

• Natural Products Industry
  (Safe, Effective, Non-GMO, Organic Products)

• Dietary Supplements
  (2/3 of Americans use Dietary Supplements)

  (Vitamins, Minerals, Herbs, Botanicals - Micrcoalgae)
Who We Are

• Cyanotech Corporation / Nutrex Hawaii, Inc.  
  (Kona, Hawaii)

• Brands
  Hawaiian Spirulina Pacifica®
  BioAstin® Hawaiian Astaxanthin®

• Grow microalgae on 90 acres @ NELHA since 1984
Who We Are
(First Crew in Kona circa 1984)
Who We Are
(1st Spirulina Manufacturing Facility)
Who We Are
(Cyanotech Manufacturing Facility – Present Date)
Consumer Protection
(Proactive Measures for Industry & manufacturers)

- FDA Regulated
  
  (3rd Party GMP Inspected & Certified since 2007)
  Mandatory Compliance 2009

- Registered Food Facility under Bioterrorism Act

- State of Hawaii Department of Health Inspected

- Consumer Complaint Monitoring–Trend Reporting
Consumer Protection
(Proactive Measures for Industry & manufacturers)

• Quality Assurance / Quality Control Dept.
  (10% of Total Company)

• Generally Recognized as Safe (GRAS)

• New Dietary Ingredient Notification (NDIN)

• Supply Chain Integration & Transparency
  (GMP Agreements with contract manufacturers)
  (Risk Assessment of new Ingredients)
Consumer Protection
(Proactive Measures – 3rd Party Certifications)

- Non-GMO Project Verification

- Gluten Intolerance Group – Gluten Free Certification

- 3rd Party GMP Certification (NPA-UL, NSF, Silliker)

- NSF Sports Certification (Banned Substances)
Consumer Protection
(Proactive Measures – 3rd Party Certifications)

• United States Pharmacopeial (USP) Dietary Supplement Verification Program (BioAstin® products in process)

• USP Monographs – Public Standard Setting Process
  (Cyanotech - Spirulina Monograph Development, 2013)
Consumer Protection
(Proactive Measures – Industry Relations)

• **Lobbying**
  (Designer Anabolic Steroid Control Act of 2014)
  (Fund FDA) – (Fund HDOH)

• **NAXA – Ingredient Trade Organization**
  (Know Your Source, safe, effective Astaxanthin from algae)
  (Monitor Market Place – Supply Chain)

• **GOED – Ingredient Trade Organization**
  (Global Organization for EPA and DHA Omega-3s)
Consumer Protection
(Proactive Measures – Industry Relations)

• United Natural Products Alliance (UNPA)
  (Cyanotech – Anchor Company in Hawaii)
  May 2016 – Annual Members Retreat, Mauna Lani
# Banned Ingredients No-Sale Policy

<table>
<thead>
<tr>
<th>Banned Ingredients</th>
<th>No-Sale Policy Effective Date</th>
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<tbody>
<tr>
<td>B-methylphenethylamine (BMPEA)</td>
<td>April 9, 2015</td>
</tr>
<tr>
<td>Bulk-powdered caffeine for retail sales</td>
<td>Feb 24, 2015</td>
</tr>
<tr>
<td>Kratom (<em>Mitragyna speciosa</em>)</td>
<td>May 1, 2014</td>
</tr>
<tr>
<td>1,3-dimethylamylamine, methylhexanamine or geranium extract (DMMA) – OXYELITE PRO</td>
<td>May 1, 2013</td>
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<tr>
<td>Ephedra or ma huang</td>
<td>May 1, 2005</td>
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</tbody>
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Consumer Protection
(Reaction – Post Market Surveillance)

• **Banned Ingredient Lists**  (CRN, NSF, UNPA)

• **FDA Import Alerts – FDA Inspections**

• **Adverse Event Reporting**  
  (Safety Call Medical Consult)

• **Recall Notification – Retailers are KEY**  
  (COMMUNICATION – COLLABORATION)
Consumer Protection
(Reaction – Post Market Surveillance)

• Industry - A Resource for Regulators & Local Officials
  (2-Way Alert System for Safety Risks & Recalls)
  (Ingredient or Test Methods Assessments)
  (Labeling & Regulatory Review & Resources)

CONSUMER PROTECTION
A SHARED GOAL