Complementary and Alternative Products

Quality: Contaminants, adulterants and substitutions

October 2021

Complementary and alternative products (CAPs) include: herbals (dried plant materials, plant extracts), dietary supplements, probiotics and homeopathic products. For most CAPs sold in New Zealand, adherence to the Code of Good Manufacturing Practice (GMP) is voluntary and regulatory approval is not needed for distribution. Analytical studies in Australia and North America, where CAPs are more regulated than in New Zealand, found less than half of CAPs purchased randomly from retail stores contained their labelled contents (1–3). A New Zealand study found 29 of 32 different fish oil capsules sold from stores had omega-3 fatty acid contents below their labelled amounts (4). This bulletin describes the problems reported regarding the quality of CAPs.

Contaminants

1. *Heavy metals e.g. arsenic, lead, mercury*

While not common, poisonings from CAPs have occurred and are usually due to heavy metal contamination. Heavy metals are used in the preparation of traditional Chinese and Indian (Ayurvedic) medicines. They can also be introduced into raw materials via water and soil pollution, or the finished product during processing (e.g. grinding) or storage (e.g. metal containers). A recent literature review (5) found 16 reports of heavy metal contamination and 12 reports of heavy metal toxicity. Six were from Ayurvedic medicines sourced from India, two involved kelp supplements and two were traditional Chinese medicines.

Key Points

Consider product quality in the risks/benefits of a patient using a CAP or if an unexpected reaction occurs

Report possible adverse reactions or interactions to CARM, and include the brand name

CAPs (or ingredients) from countries with poor food safety and pollution controls are most at risk of contamination

Adulterants are more commonly reported with CAPs promoted for weight loss, muscle-building and sexual dysfunction

2. *Microbes and parasites*

Like foodstuffs, CAPs can be contaminated with bacteria, fungi or parasites during manufacture, transport and storage due to poor compliance with GMP. This is of particular concern for immunosuppressed people e.g. transplant or oncology patients. The Food and Drug Administration (FDA) in the United States (US) analysed 138 CAPs from retail outlets (6). Bacterial contamination was highest with dried plant materials (e.g. herbal products) and lowest with vitamin and mineral supplements. FDA inspections between 2008 and 2012 found half of the 408 CAP manufacturing sites inspected had violations of GMP including unsanitary conditions and rodent infestations (7).

3. *Pesticide residues*

Pesticide use is not regulated in some countries. Several studies have found organochlorine contamination of traditional Chinese herbal products (8). An assessment of 40 CAPs in the US found 18 of them contained residues of at least one pesticide (8,9). Pesticide amounts above US tolerance levels were found in 16 products and four products contained residues of banned pesticides. Pesticide residues are unlikely to be acutely toxic but are of concern with long-term consumption.

4. Toxic plant extracts

Toxic plant extracts can be introduced into CAPs due to misidentification of plants, or poor processing of raw plant materials e.g. anthraquinones from poor processing of aloe vera. Recently, an Ayurvedic product for arthritis was recalled in Australia due to contamination with aristolochic acid (10). Aristolochic acid-containing CAPs are banned in most countries due to their association with renal cancer, but are still used in parts of Asia (11,12).

5. Stability

Like medicines, CAPs are subject to stability issues, which should be considered in manufacturing and storage. A study of 32 different fish oil capsules sold in New Zealand found the actual omega-3 fatty acid content was <67% of that labelled (4). More than three-quarters of the fish oil products tested had unacceptable levels of oxidation, thought to be occurring during, encapsulation, packing, transportation and storage.

Adulterants

Adulterants are active pharmaceuticals present in the CAP. Analysis of 49 CAPs marketed for arthritis and chronic pain in Australia, found six were adulterated with active pharmaceuticals: ephedrine, synephrine and pseudoephedrine (1). Most FDA warnings issued to manufacturers around adulteration involve products marketed for sexual dysfunction, weight loss or muscle building (12). Active pharmaceuticals found included anabolic steroids, PDE-5 inhibitors (e.g. sildenafil), diuretics, and appetite suppressants (e.g. fenfluramine and sibutramine)(12).

Substitutions

Substitution is when a cheaper raw material is used instead of the labelled ingredient e.g. rice grass substituted for *Ginkgo biloba*. Fillers such as wheat, soybean and rice may be added to the CAP but not included on the label. A DNA barcode analysis of 44 CAPs in Canada found substitution in 32% of samples and undeclared fillers in 21% (3).

References

1. Wong PHB, Harnett JE, Clases D, Wheate NJ. An Analysis for Adulteration and Contamination of Over-the-Counter Weight-Loss Products. AAPS PharmSciTech. 2021 Feb 18;22(3):78.

2. Hoban CL, Musgrave IF, Byard RW, Nash C, Farrington R, Maker G, et al. Combined Liquid Chromatography-mass Spectrometry and Next-generation DNA Sequencing Detection of Adulterants and Contaminants in Analgesic and Anti-inflammatory Herbal Medicines. Pharm Med. 2020 Feb;34(1):49–61.

3. Newmaster SG, Grguric M, Shanmughanandhan D, Ramalingam S, Ragupathy S. DNA barcoding detects contamination and substitution in North American herbal products. BMC Medicine. 2013 Dec;11(1):222.

4. Albert BB, Derraik JGB, Cameron-Smith D, Hofman PL, Tumanov S, Villas-Boas SG, et al. Fish oil supplements in New Zealand are highly oxidised and do not meet label content of n-3 PUFA. Scientific Reports. 2015 Jan 21;5(1):1–7.

5. Gyamfi ET. Metals and metalloids in traditional medicines (Ayurvedic medicines, nutraceuticals and traditional Chinese medicines). Environ Sci Pollut Res. 2019 Jun 1;26(16):15767–78.

6. Tournas VH. Microbial contamination of select dietary supplements. Journal of food safety. 2009;29(3):430–42.

7. Marcus DM. Dietary supplements: What's in a name? What's in the bottle? Drug Testing and Analysis. 2016;8(3–4):410–2.

8. Harris ESJ, Cao S, Littlefield BA, Craycroft JA, Scholten R, Kaptchuk T, et al. Heavy Metal and Pesticide Content in Commonly Prescribed Individual Raw Chinese Herbal Medicines. Sci Total Environ. 2011 Sep 15;409(20):4297–305.

9. Kutz GD. Herbal Dietary Supplements: Examples of Deceptive Or Questionable Marketing Practices and Potentially Dangerous Advice: Congressional Testimony. DIANE Publishing; 2010.

10. Administration AGD of HTG. OA/RA capsules [Internet]. Therapeutic Goods Administration (TGA). 2019 [cited 2019 Feb 25]. Available from: https://www.tga.gov.au/alert/oara-capsules

11. Han J, Xian Z, Zhang Y, Liu J, Liang A. Systematic Overview of Aristolochic Acids: Nephrotoxicity, Carcinogenicity, and Underlying Mechanisms. Frontiers in Pharmacology. 2019;10:648.

12. Gurley BJ, Yates CR, Markowitz JS. "…Not Intended to Diagnose, Treat, Cure or Prevent Any Disease." 25 Years of Botanical Dietary Supplement Research and the Lessons Learned. Clinical Pharmacology & Therapeutics. 2018;104(3):470–83.