CENTER FOR Science IN THE Public Interest

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EMBARGOED for May 15, 2017

Steven Tave, Director
Office of Dietary Supplement Programs
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Dear Director Tave:

We write to provide the Food and Drug Administration (FDA) with concerning data regarding the adulteration and marketing of ginkgo biloba supplements. We note that ginkgo has largely been shown in studies to be ineffective in achieving any significant beneficial effects for memory or circulation, and that it can increase the risk of bleeding for medical patients. Moreover, many of the supplements tested by credible laboratories show that ginkgo is frequently adulterated, and that consumers may be victims of fraud. Many consumers may fall victim to this fraud; *Nutrition Business Journal* ranked ginkgo as the 13th best seller among herbal dietary supplements in the United States in 2011, with sales of some $90 million.[1]

In fact, ginkgo may be among the most adulterated herbs sold as a supplement. We recently published an article in CSPI's *Nutrition Action Healthletter* (David Schardt, "Gingko No-Go," May 2018) (attached).[2] An expert on ginkgo adulteration who was interviewed for the article suggested that the high cost of real ginkgo leaves and its extract provides a strong incentive for intentional adulteration: "There is ample evidence of the production and sale of adulterated ginkgo extracts in the international supply chain," noted Stefan Gafner of the American Botanical Council.[3]

As we describe, an independent U.S. supplement-testing organization, ConsumerLab.com, found in its 2018 tests that 6 out of the 10 ginkgo supplements it analyzed failed quality tests.[4] The products either didn't contain much ginkgo or showed strong evidence of having been spiked with cheaper plant material. These results are consistent with ConsumerLab's prior tests of ginkgo supplements purchased in the United States. In 2003, 7 of 9 ginkgo products, and in 2008, 5 of 7 products, showed signs of adulteration. In addition, a U.S. Department of Agriculture 2012 study showed that at least 7 of the 18 gingko supplements it analyzed were adulterated.[5]

We encourage your office to review the attached January 2018 Botanical Adulterants Bulletin prepared by the American Botanical Council, the American Herbal Pharmacopoeia, and the University of Mississippi's National Center for Natural Products Research about the adulteration of ginkgo biloba supplements, and to obtain ConsumerLab's detailed testing and product results directly from the company, which makes them available for a modest

subscription fee ($42 per year for individuals). In general, insofar as it does not already do this, ODSP should adopt a practice of regularly examining the results of ConsumerLab's testing, or the results from other independent laboratory testing published by researchers, which would allow the FDA to better monitor whether supplements that are commonly sold and marketed to consumers are adulterated. In the specific case of ginkgo adulteration, the agency should act, since the evidence of intentional adulteration in U.S.-sold products is clear.

Ginkgo's problems are not limited to the United States. In Germany in 2010, only 3 of 10 ginkgo supplements passed authenticity tests.[6] In 2016, Canadian researchers found that only 4 of 14 ginkgo products obtained from Canadian suppliers were *not* adulterated with filler.[7] In the United Kingdom, only 2 of 35 ginkgo supplements purchased in London in 2016 were not adulterated.[8] Of 18 supplements purchased in North America and Europe between 2015 and 2017 and tested by NSF International, only 3 contained authentic ginkgo.[9] And in a new analysis published last month, European researchers tested ginkgo products sold in the European Union and concluded that their quality was "dubious."[10]

A frequent substitution material appears to be buckwheat, which contains rutin and can cross-react with ginkgo in bioassays. As a recent bulletin by a group of herbal trade associations notes, the pattern strongly suggests that there is a widespread and common practice of intentional adulteration that is designed to evade testing in the supply chain:

> According to William Obermeyer, PhD, former FDA natural products chemist and former technical director of ConsumerLab.com, the costs for a *Ginkgo biloba* extract in 2009 varied between $35-90/kg, while the price of rutin isolated from buckwheat is ca. $10/kg, giving an incentive for adulteration to unscrupulous suppliers and manufacturers.[11]

The same researcher noted in a 2008 article in *Natural Products Insider* that the quality of ginkgo products likely grew worse from 1999 to 2007.[12]

In addition, the FDA should closely examine the claims being made on labels and in related materials about ginkgo biloba to ascertain whether they are supported by sufficient evidence. Many of the products, including those tested by ConsumerLab, make claims that ginkgo's effects include "promot[ing] mental function and memory."[13] In a study financed by the National Institutes of Health (NIH), U.S. researchers gave 3,069 men and women aged 75 and older 240 mg of authentic ginkgo or a placebo to take every day. Over six years, those taking ginkgo were just as likely as the placebo takers to be diagnosed with dementia.[14] Furthermore, among those who did not develop dementia, taking ginkgo failed to slow decline in memory, attention, use of language, visuospatial abilities, or executive function (planning and organizing) relative to the placebo.[15]

While there is no similarly well-designed long-term trial in younger people testing the effect of ginkgo on memory or other cognitive abilities, researchers in the United Kingdom

pooled the results of 13 smaller studies that included 4 trials in people under the age of 45. They also found that, across those studies, ginkgo had no more impact on memory, attention, or executive function than a placebo.[16]

Other uses of ginkgo are equally unsupported by evidence. While some people with intermittent claudication—aches and cramps caused by poor circulation in the legs—claim that ginkgo relieves the pain of walking, a 2013 Cochrane Collaboration review of 11 clinical trials found little to support such claims.[17] Overall, the authors concluded that there is no "evidence that Ginkgo biloba has a clinically significant benefit for patients with peripheral arterial disease."

Taking ginkgo biloba also poses some risk. The National Institutes of Health cautions that those who are "older, have a known bleeding risk, or are pregnant…should be cautious about ginkgo possibly increasing your risk of bleeding,"[18] Given these concerns, the FDA should also consider whether requiring a warning on packages for ginkgo biloba products is warranted.

Adulterated products, sadly, also pose modest risks. While the extracts and substances used to adulterate ginkgo are not known to pose a health risk, these are not clinically tested ginkgo products and, as a result, the risks may be poorly explored or unknown. As the bulletin notes: "[i]n addition, adulterated low quality ginkgo extracts may contain higher concentrations of less desirable ginkgo leaf constituents, *e.g.*, ginkgolic acids, which are known contact allergens and have been shown to cause contact dermatitis."

We would be interested in speaking with you at your convenience concerning our ongoing interest in monitoring the integrity, safety, and efficacy of the supplement marketplace more generally.

With best wishes,

Laura MacCleery
Director, Regulatory Affairs
Center for Science in the Public Interest

Notes

[1] Ginkgo biloba. NBJs Supplement Business Report. New York City, NY: Penton Media; 2012;198.
[2] Schardt D, Ginkgo No-go: Filler, Anyone? *Nutrition Action Healthletter*, 2018 May. Available by subscription at: https://cspinet.org/nutrition-action-healthletter.
[3] Stefan Gafner, Adulteration of *Ginkgo biloba* Leaf Extract. Botanical Adulterants Bulletin, 2018. (Accessed online at: http://cms.herbalgram.org/BAP/pdf/BAP-BABs-Ginkgo-CC-V2b.pdf).
[4] *See* www.Consumerlab.com.
[5] Harnly JM, *et al*, Detection of adulterated Ginkgo biloba supplements using chromatographic and spectral fingerprints. J AOAC Int. 2012 Nov-Dec; 95(6):1579-87.
[6] Tawab M, *et al*, Dietary supplements with ginkgo under the microscope. Pharm Ztg. 2010;20:62-67.
[7] Ma YC, *et al*, An effective identification and quantification method for Ginkgo biloba flavonol glycosides with targeted evaluation of adulterated products. Phytomedicine. 2016 Apr 15;23(4):377-87.
[8] Booker A, *et al*, Adulteration and poor quality of Ginkgo biloba supplements. Journal of Herbal Medicine. 2016;6(2):79-87. (Accessed online at https://www.sciencedirect.com/science/article/pii/S2210803316300239).
[9] This assertion is grounded in an unpublished study cited by the Gafner monograph, *supra* note 10, and based on an email to CSPI from NSF International. The FDA could ask the NSF for the study, if needed.
[10] Czigle S, *et al*, Ginkgo biloba Food Supplements on the European Market - Adulteration Patterns Revealed by Quality Control of Selected Samples. Planta Med. 2018 Apr;84(6-07):475-482.
[11] *Id.*; Obermeyer W. Economically motivated adulteration in the dietary supplement marketplace. Public Meeting on Economically Motivated Adulteration; 2009. College Park, MD.
[12] Myers S. Adulteration stifles the Ginkgo biloba Market. *Natural Products Insider* 2008:38-41.
[13] *See* Doctor's Best "Extra Strength Ginkgo" product depicted in Schardt D, Ginkgo No-go: Filler, Anyone? *Nutrition Action Healthletter*, 2018 May. Available by subscription at: https://cspinet.org/nutrition-action-healthletter.
[14] DeKosky S, *et al*, Ginkgo biloba for prevention of dementia: a randomized controlled trial. JAMA. 2008 Nov 19;300(19):2253-62.
[15] Snitz BE, *et al*, Ginkgo biloba for preventing cognitive decline in older adults: a randomized trial. JAMA. 2009 Dec 23;302(24):2663-70.
[16] Laws KR, *et al*, Is Ginkgo biloba a cognitive enhancer in healthy individuals? A meta-analysis. Hum Psychopharmacol. 2012 Nov;27(6):527-33.
[17] Cochrane Database Syst. Rev 6: CD006888, 2013. (Accessed online at: https://www.ncbi.nlm.nih.gov/pubmed/23744597).
[18] National Center for Complementary and Integrative Health: Ginkgo. 2016.