Kava: a test case for Canada's new approach to natural health products

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In this issue, Edward Mills and colleagues[1] report the results of a study in which simulated customers asked employees at 33 health food stores to recommend a treatment for anxiety. Even though herbal kava had been the subject of a Health Canada advisory,[2] employees in 22 (67%) of the 33 stores recommended kava. The simulated customers returned to the same stores 2 months after Health Canada issued a stop-sale order for products containing kava[3] and found that 17 (57%) of the 30 stores still in business continued to sell it. These findings should be of concern to health care professionals and consumers alike. The study by Mills and colleagues[1] raises the questions of how Health Canada can enforce its position on natural health products and what the impact on the health of Canadians might be if stop-sale orders are ignored. Kava represents an important test case with respect to Health Canada's approach to natural health products, and thus it is important to place its story in the context of the evolving regulations governing natural health products in Canada.

Kava (*Piper methysticum*) is a herbal product commonly used to manage symptoms associated with anxiety. Several reviews of the scientific evidence from randomized, placebo-controlled, double-blind studies have concluded that kava is an effective treatment for anxiety.[4–7] The recommended dose is 100 mg of kava extract (standardized to contain 70% kavalactones) given 2 or 3 times per day,[8] but the receptor targets and mechanism of action are not known. Until 2002, kava was generally considered a safe herb with minimal adverse effects. However, 25 case reports of serious toxic effects on the liver, including cirrhosis, hepatitis and liver failure, associated with kava use in Germany and Switzerland,[2] as well as the case of a woman requiring a liver transplant in the United States,[9] raised concerns about the safety of kava. After reviewing the international evidence and identifying 4 suspected cases of liver toxicity associated with kava use in Canada, Health Canada issued a stop-sale order for all products containing kava on Aug. 21, 2002.[3] Products containing kava were at that time available under Canadian food or homeopathic drug regulations, which meant that consumers could purchase them without consulting a health care provider and manufacturers did not have to put warnings on the product labels. In its August 2002 stop-sale order, Health Canada stated that there were "no acceptable food uses for kava" and announced that kava products were to be regulated as conventional drugs in the future.[3] It is important to note that Health Canada did not "ban" kava, as was widely reported.

Several criticisms of the evidence for kava hepatotoxicity have been raised.[10,11] All of the data come from case reports, which are generally considered a weak form of evidence. Some of the cases may have been reported and counted more than once, and most of the patients were taking other potentially hepatotoxic drugs, which makes it difficult to determine causality. Data on concurrent alcohol consumption were often unavailable. Liver toxicity generally occurred 2 to 3 months after kava intake (a relatively long period between exposure and effect), and many case reports did not indicate the duration of kava use. Finally, different types of kava extract, as well as a synthetic kavain (a component of kava), are sold, which further complicates interpretation of the case reports. Of 68 suspected cases reviewed by Ernst,[10] 14 were assessed as probably being caused by kava and 14 as possibly being caused by kava, including 3 severe cases that resulted in the need for a liver transplant or death. However, as noted by Stevinson and associates,[12] 2 postmarketing surveillance studies did not identify liver toxicity among a total of 7978 patients taking 150 to 240 mg kava extract daily for approximately 6 weeks.

Health Canada's 2002 decision to reclassify kava as a conventional drug appears prudent, given concerns about liver toxicity, even if this side effect is rare. Kava is clearly not eaten as a food, and even low rates of liver toxicity are not acceptable for any food. The decision means that manufacturers selling kava in the future must empirically demonstrate the safety of kava to gain approval under Canadian drug regulations. However, another avenue will become available to manufacturers of kava products in January 2004, when new natural health product regulations come into effect, under the auspices of the Natural Health Products Directorate of Health Canada.[13] Kava may be eligible for return to the Canadian market under these regulations, provided the safety concerns can be

mitigated through appropriate use of warning labels or other measures.

The sale of kava in health food stores 2 months after a stop-sale order, as reported by Mills and colleagues,[1] reflects the confusion surrounding the regulation of herbs and its enforcement and suggests the need for regulation not only of the products themselves, but also at the point of sale. Informing consumers of the potential risks of nonprescription pharmaceuticals through product labelling is a good idea, but the differing opinions on the evidence of kava toxicity demonstrate that the assessment of risks and benefits can be complex, and it might be a considerable challenge to adequately equip the public to make informed decisions about whether or not to use such products. We hope that the new regulatory framework for natural health products will balance the need to protect Canadians from unsafe compounds and preparations with the freedom of individuals to make autonomous health care decisions.

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