EDITORIAL

Alternative medicine products causing acute liver injury: Pandora's box is open

Fanny Bergeron MD, FRCPC[1], Trana Hussaini PharmD[2], Natasha Chandok MD, MPH, FRCPC[3,4,5], Eric M Yoshida MD, FRCPC[6,7]

ABSTRACT

The regulatory loopholes governing alternative medicine products in Canada represent a public safety issue. In 2017 and 2018, the Liver Transplant Program of the University of British Columbia assessed three patients with acute liver failure secondary to alternative medicines. As health care professionals, we have a duty to both recognize the magnitude of the problem and advocate for reform of the current regulatory process for alternative medicine products.

KEY WORDS: acute liver injury; alternative medicine; drug-induced liver injury; herbal products; liver transplant; natural health products

Author Affiliation

[1]*Division of Gastroenterology, Vancouver General Hospital, Vancouver, British Columbia;* [2]*Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, British Columbia;* [3]*Department of Medicine, Division of Gastroenterology, William Osler Health Centre, Brampton, Ontario;* [4]*Adjunct Professor of Medicine, University of Western Ontario, London, Ontario;* [5]*Clinical Affiliate, University of Manitoba, Winnipeg, Manitoba;* [6]*Department of Hepatology, Vancouver General Hospital, Vancouver British Columbia;* [7]*Division of Gastroenterology, University of British Columbia, Vancouver, British Columbia*

Correspondence: Eric M Yoshida, Vancouver General Hospital, Gordon and Leslie Diamond Health Care Centre, 5th floor, 2775 Laurel Street, Vancouver, British Columbia V5Z 1M9. Telephone: 604-875-5371. Fax: 604-875-5447. E-mail: eric.yoshida@vch.ca

Alternative medicine use is a rising trend in the Western world and represents a multi-billion-dollar industry. In 2010, 73% of Canadians regularly consumed natural and herbal products (1). With the exponential growth of the market over the past decade, we can only estimate that this proportion has grown further. Despite government attempts at regulation, the majority (59%) of herbal medicines sold in North America contain unlabelled ingredients, including prohibited pharmaceutical drugs or toxic agents such as heavy metals (2,3). Globally, natural health products have minimal regulatory requirements compared with prescription drugs (4) Health Canada is currently initiating a long overdue reform of the regulatory process to protect the health of Canadians, but the task ahead is tremendous in scope and complexity and will be onerous to achieve (5). In the meantime,

OPEN ACCESS

too often the public is fed a false perception that these alternative medicines are safe and efficacious. Efficacy concerns aside, at present the composition and appropriate dosing of alternative medicines are unclear to consumers, and access to these products is unrestricted. For this reason, there is a dire and unmet need for policies to protect the public from these agents.

Case in point: in 2017 and 2018, the Liver Transplant Program of the University of British Columbia assessed three patients with acute liver failure secondary to alternative medicines (6). Tragically, one of the patients did not survive after transplant. The other patient was successfully transplanted and the third recovered without the need for transplantation. At the time these patients were transferred to our centre, the etiology of acute liver failure was still unclear; however, all liver biopsies revealed drug-induced liver injury. All three patients had previously been healthy and were taking no hepatotoxic prescription drugs. However, careful history taking revealed they were all traditional herbal-medicine consumers. The products involved were traditional herbal medicines from China, India, and Japan sold commercially in Canada. We analyzed one of the products in our chemistry laboratory and found the presence of large concentrations of unlabelled ingredients such as nimesulide, a non-steroidal anti-inflammatory drug neither approved nor marketed in Canada due to safety concerns.

The real tragedy is that these devastating cases could have been avoided if there had been effective regulation of alternative medicines. It illustrates how unlicensed—and therefore prohibited—pharmaceuticals may become commercially available in Canada via a regulatory loophole governing herbal products, with potentially tragic outcomes. Thus, there is an urgent need for governmental regulation and consumer safety policies regarding the manufacture, importation, and dispensing of herbal and natural products to prevent further tragedies. It is our personal view—and we emphasize that we do not speak for any organization, including the Canadian Association for the Study of the Liver (CASL)—that Health Canada needs to hold the alternative medicine product industry to the same standard as it does the pharmaceutical industry. We note that a recent review commented on the lack of adequate regulation in both the United States and Europe; therefore, Canada is not alone in this lack of governmental regulation (7).

From a public safety perspective, it needs to be recognized that these widely available products can result in hepatotoxicity that may require hospitalization, urgent liver transplantation, and may even result in mortality. We also believe that hepatotoxicity from these products may be more common than has previously been thought: a recent review of drug-induced liver injury (DILI) associated with Traditional Chinese Medicine (TCM) products in China reported that DILI associated with TCM constituted 25% of all DILIs reported (8). We also note that a recent research symposium of the American Association for the Study of Liver Disease and the National Institutes of Health revealed that 20% of reported cases of hepatotoxicity in the United States might be due to herbal and dietary supplements (9). The public needs to be made aware that there is a real risk associated with natural, herbal, and alternative medicine products and that Canadian regulators have a duty to protect the public from needless harm as well as to educate the public of the potential risk. As health care professionals, we have an obligation to both recognize the magnitude of the problem and advocate for reform of the current regulatory process.

CONTRIBUTIONS: Conceptualization, FB, EY; Investigation, FB, TH, NC, EY; Writing – Original Draft, FB, NC, EY; Writing – Review & Editing, FB, TH, NC, EY; Supervision, TH, NC, EY.
FUNDING: No funding was received for this work.
DISCLOSURES: The authors have nothing to disclose.

REFERENCES

1. Health Canada; Ipsos-Reid. Natural health product tracking survey, 2010: final report. HCPOR-09-25. Ottawa: Health Canada; 2010. http://epe.lac-bac.gc.ca/100/200/301/pwgsc-tpsgc/por-ef/health/2011/135-09/report.pdf (Accessed January 16, 2019).
2. Newmaster SG, Grguric M, Shanmughanandhan D, Ramalingam S, Ragupathy S. DNA barcoding detects contamination and substitution in North American herbal products. BMC Med. 2013;11:222. https://doi.org/10.1186/1741-7015-11-222. Medline: 24120035
3. Farrington R, Musgrave I, Nash C, Byard RW. Potential forensic issues in overseas travellers exposed to local herbal products. J Forensic Leg

Med. 2018;60:1–2. https://doi.org/10.1016/j.jflm.2018.08.003. Medline: 30149301

4. Stanbrook M. Natural health products should be sold separately from drugs. CMAJ. 2017:189(25):E848. https://doi.org/10.1503/cmaj.170661. Medline: 28652478
5. Health Canada. Consulting Canadians on the regulation of self-care products in Canada [Internet]. Ottawa: Government of Canada; c2016 [updated 2016 Nov 25]. Available from: https://www.canada.ca/en/health-canada/programs/consultation-regulation-self-care-products/consulting-canadians-regulation-self-care-products-canada.html (Accessed November 4, 2018).
6. Yoshida EM, Hussaini T, Cooper P, et al. Herbal medicine and liver toxicity. BCMJ. 2017;59(7):348 [Lett]. https://www.bcmj.org/letters/herbal-medicine-and-liver-toxicity.
7. Navarro VJ, Lucena MI. Hepatotoxicity induced by herbal and dietary supplements. Semin Liv Dis. 2014;34(2):172–93. https://doi.org/10.1055/s-0034-1375958. Medline: 24879982
8. Wang R, Qi X, Yoshida EM, et al. Clinical characteristics and outcomes of traditional Chinese medicine-induced liver injury: a systematic review. Expert Rev Gastroenterol Hepatol. 2018;12(4):425–34. https://doi.org/10.1080/17474124.2018.1427581. Medline: 29323538
9. Navarro VJ, Khan I, Björnsson E, Seeff LB, Serrano J, Hoofnagle JH. Liver injury from herbal and dietary supplements. Hepatology. 2017;65(1):363–73. https://doi.org/10.1002/hep.28813. Medline: 27677775