Although the investigators presented important information (e.g., that St. John’s Wort extracts and grapefruit juice affect the metabolism of many drugs used by cardiologists), the bulk of the report appears to be a collection of medical database “hits”; one-third of the herbs identified are rarely or never present in the U.S. marketplace. The investigators also stray from their central purpose by opining on diverse topics outside the scope of their expertise, such as quality control, advertising, and basic dietary supplement regulation.

Reported problems regarding botanicals include, for example, that “colchicine has been found in the placenta of women taking ginkgo” (1), an erroneous finding that has been soundly discredited (3–5). Similarly, in their discussion of ginseng, the investigators state that “neonatal death has been related to maternal use” (1). However, the material consumed in this case of neonatal androgenization (not death) was reported in the cited reference as not a true ginseng, not “Siberian ginseng” (as stated in the original report), but confirmed by Canadian government researchers as Chinese silk vine (6,7).

Additionally, although the investigators claim in an unreferenced statement that products made from the herb black cohosh “inhibit CYP3A4 and potentially increase the risk of adverse effects from some drugs” (1), the fact is that although 1 in vitro study indicated this possibility, 3 others, including 2 human studies, have confirmed that no such inhibition is associated with this herb (8–10).

Clinically significant information about how herbs affect drug metabolism, particularly patients on digoxin or warfarin, is important to cardiologists. However, the investigators do not provide references for dozens of their assertions in this area, and they get the facts wrong in several places in which they do provide references.

Although the investigators’ intent is appreciated, it is important that the review and dissemination of safety information on herbs be held to the same standards found in any other field of scientific endeavor (11). In the interest of patient safety and provider education, the American Herbal Products Association published the Botanical Safety Handbook in 1997 (12). A thoroughly revised edition will be available in the near future, with the hope that it will be recognized as a valuable tool for credible and up-to-date information on the safety of herbs.

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Herbal Products Review Provides Inaccurate Information on Dietary Supplement Regulations

Tachjian et al. (1) fail to present a meaningful review of the challenges of herbal supplement use in patients with cardiovascular disease. Instead, they present outdated and incorrect information and make sweeping generalizations about herbal products and dietary supplements in general. As a result, the reader is no better equipped to manage patient care. This is unfortunate, because the potential for drug–herb interactions is a critical topic and is clinically relevant for practicing cardiologists, as 24% of consumers have reported using herbal supplements (2), with few patients discussing this supplementation with their health care professionals. Those patients willing to discuss herbal use with their physicians often project distrust of medicine when natural products are too eagerly dismissed.

One apparent purpose of the review was to highlight what are perceived by the investigators as regulatory shortfalls of the dietary supplement industry. However, they lack a fundamental understanding of the regulatory requirements. Herbal supplements are considered dietary supplements as defined in the Dietary Supplement Health and Education Act of 1994 (DSHEA) (3), which provides a regulatory framework distinct from that for conventional foods or drugs. In their review, the investigators make numerous references to products that are not herbal dietary supplements or are not commonly available. It is unclear, for example, why a review on herbal supplements would highlight drug interactions with grapefruit juice, a food. In claiming a lack of government oversight, the investigators state that “the only requirement is for the manufacturer to send a copy of the product label to the U.S. Food and Drug Administration (FDA)” (1). Although there are numerous requirements in place for herbal dietary supplements, submitting a label to the FDA is not among them. The investigators
continue, “A new dietary supplement . . . can be introduced and marketed overnight . . . despite containing new, experimental, and unregulated herbal ingredients” (1). Again, this statement is false.

If a manufacturer wishes to market a product that contains a new herbal ingredient, there is a new dietary ingredient 75-day premarket notification process in which safety data are supplied to the FDA for review (4). Similarly, the investigators claim that manufacturers are “exempt . . . from any post-marketing surveillance” (1), while in reality, this responsibility is assigned to both the FDA and the Federal Trade Commission. Furthermore, the investigators suggest that manufacturers do not comply with adverse event reporting law, noting that “between 1990–94, fewer than 10 of more than 2,500 reports of adverse effects made to the FDA came from herbal product manufacturers” (1). These data, which predate both the law requiring the reporting of serious adverse events (2006) and DSHEA (1994), present a skewed view of industry compliance.

The investigators suggest a lack of regulation whereby an herbal ingredient can be introduced to the market without restriction, no post-market surveillance is conducted, and herbs present a disproportional risk to patients. DSHEA, serious adverse event reporting, and good manufacturing practices for dietary supplements, introduced by the FDA in 2007 but mandated by DSHEA in 1994, provide a strong and appropriate regulatory framework for the dietary supplement industry in the U.S. Despite these advances, potential drug-herb interactions will continue to present challenges to practicing clinicians. Thus, to meet patients’ expectations, clinicians need a clear and factual presentation of the regulatory background of herbal supplement products and a thoughtful evaluation of defined and theoretical contraindications and drug interactions affecting patients being treated for cardiovascular diseases. This review is a step backward in opening up a dialogue between clinicians and patients on the topic of herbal products.

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We thank Drs. Asher, Dentali, and Chaudhry for their interest in our review (1) and for their critical comments. The intent of our review, written for cardiologists and other health care providers, was to provide practical information about issues related to the use of herbal products in patients with cardiovascular diseases. We presented the information in easy-to-follow language, minimizing technical jargon, to remind busy practicing physicians to ask their patients about the use of herbal products that could potentially increase adverse drug reactions, including catastrophic events, such as major bleeds, transplanted organ rejection, predisposition to life-threatening arrhythmias, or reductions in the efficacy of medications used. The review has been received with great enthusiasm from practicing cardiologists and other health care providers but also has generated criticism, mainly from practitioners and from supporters and manufacturers of herbal products.

We thank Dr. Dentali for his comments regarding the importance of doctor–patient communication and the need for education about herbal products, and we appreciate the efforts of the American Herbal Products Association to educate the public about their use. We were surprised at and disappointed in the comments regarding our discussion of issues such as a lack of quality control, advertising (public misinformation arising from the promotion of supplements without scientific evidence for their efficacy and safety), and the regulation of herbal supplements, which have direct implications for public health. Dr. Dentali’s statement about the report on colchicine in the placentas of women taking gingko (2) being erroneous is not discredited by the citations provided. In our review, we did not raise the issue of whether colchicine can be found naturally in ginkgo but in the context of quality control, contamination, and adulteration of herbal products (1). In the report we cited (2), colchicine was identified by sophisticated analytical techniques in placental blood from 5 women who used herbal supplements but not from 19 nonusers. A significant amount of colchicine (26 ± 3 µg/tablet) was also detected in ginkgo biloba purchased from a local market in the Detroit area. In the Li et al. (3) study, cited by Dr. Dentali, ginkgo biloba purchased from pharmacies in Chicago did not reveal any significant colchicine levels. These findings and other studies indicate an absence of colchicine in naturally occurring ginkgo but do not rule out contamination or adulteration, an issue reported with several herbal products (4–12). The information on the neonatal death is from a monograph on ginseng prepared by the Natural Standard Research Collaboration (13) and is available at the Medline Plus website, a service of the U.S. National Library of Medicine and the National Institutes of Health. We apologize for the confusion from this report that we cited and are thankful to Dr. Dentali for pointing out the issue of mislabeling (likely adulteration) of Chinese silk vine (Periploca sepium) sold as Siberian ginseng (14). The effect of black cohosh on cytochrome P450 (CYP) 3A4 has been demonstrated by several investigators (15–17) and the constituents of the commercially available black cohosh (Cimicifuga racemosa) that causes the inhibition of human CYP 3A4 identified (15) as triterpene glycosides with weak effect and fukinolic acid and cimicifugic acids A and B as strong inhibitors of 4 CYP isozymes (1A2, 2D6, 2C9, and 3A4) (16). The inhibitory effect of black cohosh was again confirmed recently by Sevior et al. (17). The reason for the discrepancy in the reports cited by Dr. Dentali is unclear. The Dietary Supplement Information Expert Committee