



SPECIAL FEATURE

Natural \neq Safe: Spine Care Provider's Guide to Herbal Supplements

*Poison is in everything, and no thing is without poison.
The dosage makes it either a poison or a remedy.*

Philippus Aureolus Paracelsus (1493-1541) German-Swiss Physician¹

David A. Wong, MD, MSc, FRCS(C)
President, NASS
Co-chair, NASS Patient Safety Task
Force
Denver Orthopedic Clinic
Denver, CO

In addition to benefits, herbs—like prescription medications—can have unwanted side effects, cause drug interactions and possibly create surgical problems. Large doses of herbs (the belief that “if one is good, more must be better”) can be dangerous. Many herbs have pharmacologic effects on the body.

In October 2002, NASS launched an herbal patient safety program which included physician education, a patient education brochure and patient history checklist. Much of the physician education document is reprinted here from the NASS publication by the same name. The complete document, including 18 pages of herbs with their uses/effects, potential side effects and potential interactions, can be ordered.

The information provided in this document should be considered a general overview. It is not all inclusive and is provided for information and education only. This document should not be construed as including all proper methods of care or excluding other acceptable methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding any treatment is to be made by the physician in light of circumstances presented by the patient and the needs and resources particular to the locality or institution.

Alternative medicine is becoming an accepted and prominent part of the spectrum of medical treatments available to patients today. Most US medical schools offer alternative medicine courses and many insurers are offering alternative medicine programs and benefits.^{2,3} Visits to alternative therapy practitioners exceeded projected visits to primary care physicians in 1997.⁴

One of the most common forms of alternative medicine is the use of herbal supplements. Patients are self-medicating with over-the-counter herbals (considered a form of dietary supplement) in greater numbers than

ever before. Consumer spending for dietary supplements and functional foods was estimated at approximately \$31 billion in 1999 by Congress' General Accounting Office.⁵

“Natural” Doesn't Always Mean Safe

In addition to benefits, herbs—like prescription medications—can have unwanted side effects, cause drug interactions and possibly create surgical problems. Large doses of herbs (the belief that “if one is good, more must be better”) can be dangerous. Many herbs have pharmacologic effects on the body.⁶ The many chemical components in herbal products may have variable concentrations based on plant genetics, plant parts and growing conditions. Herbs' multiple components may also interact differently based on harvesting practices, processing or packaging. Contamination also can take place during production.⁷ For example, heavy metal contamination has been found in some Asian herbal remedies.

Even herbs that are generally safe can be dangerous or have side effects under the wrong conditions. For instance, botanicals can interact with anesthesia or other medications commonly used in surgery or the procedure itself, causing surgical complications.⁶ Some herbs may enhance bleeding. Nonsurgical drug-herb interactions are also common. Approximately 15 million adults are at risk for potential adverse interactions between prescription medicines and herbs or high-dose vitamins.⁴ More than 2,900 reports of adverse events (including 104 deaths) involving supplements have been made to the Food and

Drug Administration (FDA). The FDA estimates that for each report it receives, 100 more go unreported.⁵

Who Uses Herbals and Why?

In a study⁴ of alternative medicine trends in the US between 1990 and 1997, alternative treatments were most often used for chronic conditions, including back problems, anxiety, depression and headaches. A recent study⁸ of 2,560 elective noncardiac surgery patients in California determined that:

- 39.2% of patients surveyed admitted to using alternative medicine supplements, with herbals being the most common.
- Of those taking supplements, 44.4% did not consult their primary physician and 56.4% did not tell their anesthesiologist before surgery.
- 53% stopped usage before surgery.

The study also described factors associated with the preoperative use of herbals, which included:

- female
- age 35-49
- higher income
- Caucasian
- higher education
- sleep problems
- joint or back problems
- allergies
- addiction problems
- history of general surgery

Herbal use may also be more prevalent among certain populations and their descendants, including Asians (use of herbals), Indians (Ayurvedic medicine practices), Native Americans, Africans, people from the Caribbean, Central and South America, those of Appalachian origin, seniors (age >65), college-age athletes (bodybuilding/athletic performance) and young women (weight loss and menstrual complaints), cancer patients or those with AIDS.^{6,7,9}

Patient Disclosure and Sources of Information

Key to preventing adverse events is knowing what herbals patients are taking, but a large percentage of patients are not

likely to tell their physicians about herbal supplement use. Patients may not readily disclose herbal use because they believe physicians are ill-informed or don't support the use of herbs, believe it is unrelated to their medical care or don't believe the supplements to be medications.

likely to tell their physicians about herbal supplement use. Patients may not readily disclose herbal use because they believe physicians are ill-informed or don't support the use of herbs, believe it is unrelated to their medical care or don't believe the supplements to be medications.^{10,11,12} In addition, many patients do not get information on herbs from their health care providers. According to a *Prevention* magazine survey, major sources of supplement information are friends and family, magazines, product labels and advertising.⁵

Regulation

Overview. Herbs are considered dietary supplements. The FDA regulates dietary supplements under a different set of regulations than those covering conventional food and drug products (prescription and over-the-counter). Under the Dietary Supplement Health and Education Act of 1994 (DSHEA), the dietary supplement manufacturer is responsible for ensuring that a dietary supplement is safe before it is marketed. The FDA is responsible for taking action against any unsafe dietary supplement product after it reaches the market. Generally, manufacturers do not need to register with the FDA or get FDA approval before producing or selling dietary supplements. Manufacturers must make sure that product label information is truthful and not misleading.

The FDA's postmarketing responsibilities include monitoring safety, eg, voluntary dietary supplement adverse event reporting and product information, such as labeling, claims, package inserts and accompanying literature. The Federal Trade Commission (FTC) regulates dietary supplement advertising.¹³

What is a Dietary Supplement? Congress

defined the term "dietary supplement" in the 1994 DSHEA as: a product taken by mouth that contains a "dietary ingredient" intended to supplement the diet. The "dietary ingredients" in these products may include: vitamins, minerals, herbs or other botanicals, amino acids and substances such as enzymes, organ tissues, glandulars and metabolites. Dietary supplements can also be extracts or concentrates and may be found in many forms such as tablets, capsules, softgels, gelpcaps, liquids or powders. Whatever their form, the 1994 DSHEA places dietary supplements in a special category under the general umbrella of "foods," not drugs, and requires that every supplement be labeled a dietary supplement.¹⁴

Regulation Information. Before October 1994 when the DSHEA was signed into law, dietary supplements were subject to the same regulatory requirements as other foods. This new law, which amended the Federal Food, Drug and Cosmetic Act, created a new regulatory framework for the safety and labeling of dietary supplements.

Under the DSHEA, firms are responsible for determining that dietary supplements they manufacture or distribute are safe and that any representations or claims made about them are substantiated by adequate evidence to show they are not false or misleading. Dietary supplements do not need approval from the FDA before they are marketed. Except in the case of a new dietary ingredient, where premarket review for safety data and other information is required by law, a firm does not have to provide FDA with the evidence it relies on to substantiate safety or effectiveness before or after it markets its products. Also, manufacturers do not need to register themselves nor their dietary supplement products with the FDA before producing or selling them. Currently, there are no FDA



Comparison of Prescription Medications, Over-the-Counter Medications and Herbal Supplements

	Prescription Medications	Over-the-Counter (OTC) Medications	Herbal Supplements
Description	Drug products that require a doctor's authorization.	Drug products available without a doctor's prescription. Includes products that may not be associated as drugs, such as fluoride toothpaste, dandruff shampoos and sunscreens.	Dietary supplements (under the general umbrella of foods, not drugs). Regulated under different rules than prescription and OTC medications.
Regulation	Regulated by the FDA. All new drugs must be proven effective and safe before they can be approved by the FDA for marketing. The FDA evaluates studies submitted by the drug's sponsor for safety and effectiveness for its intended use. A proposed drug's benefits must outweigh known risks.	Regulated by the FDA. Many OTCs were available for years prior to laws requiring proof of safety and effectiveness before marketing. The FDA evaluates ingredients and labeling through the OTC Drug Review Program, creating monographs for each product class. Monographs cover acceptable ingredients, doses, formulations and labeling. Products conforming to monographs may be marketed without FDA clearance; those that don't must be approved through the new drug approval system. Must be safe and effective for self-use. Proposed drug's benefits must outweigh known risks.	Manufacturer is responsible for ensuring safety before market. Generally, manufacturers do not need to register with the FDA or get FDA approval before production or sale.
Monitoring	The FDA monitors use of marketed drugs for unexpected risks and takes action when they are detected. Evaluates regular reports from manufacturers.	The FDA monitors use of marketed drugs for unexpected risks and takes action when they are detected. Evaluates regular reports from manufacturers.	Manufacturers/distributors are not required to record, investigate or forward to the FDA reports of injuries or illnesses related to products. The FDA is responsible for taking action against unsafe products after they reach market.
Manufacturing Practices and Content	The FDA works with pharmaceutical companies to assure all drugs marketed in the US meet specifications for identity, strength, quality, purity and potency. Manufacture of drugs and standards of drug quality are regulated by the FDA.	FDA OTC monographs cover acceptable ingredients, doses, formulations and labeling. The manufacture of drugs and standards of drug quality are regulated by the FDA.	No FDA regulations establish a minimum standard of practice of manufacturing. Other than manufacturer responsibility for safety, no rules to limit a serving size or the amount of nutrient.
Claims and Labeling	The FDA regulates proper labeling and advertising. Advertisements and labeling must be truthful and not misleading.	Clear and truthful labeling is required, written so that ordinary people are able to easily find and understand information. Advertising is regulated by the Federal Trade Commission.	Cannot be promoted as a treatment, prevention or cure for a specific disease or condition. Only three claims allowed: health claims, structure/function claims and nutrient content claims. Manufacturers must ensure label information is truthful and not misleading. The Federal Trade Commission regulates advertising.



regulations specific to dietary supplements that establish a minimum standard of practice for manufacturing. At present, the manufacturer is responsible for establishing its own manufacturing practice guidelines to ensure that the dietary supplements it produces are safe and contain the ingredients listed on the label. Other than a manufacturer's responsibility to ensure safety, there are no rules that limit a serving size or the amount of nutrient in any form of dietary supplement.

Unlike drug products, dietary supplement manufacturers and distributors are not currently required by law to record, investigate or forward to the FDA any reports of injuries or illnesses that may be related to use of their products. Once the product is marketed, however, the FDA has the responsibility for showing that a dietary supplement is unsafe before it can take action to restrict the product's use or removal from the marketplace. Except for rules governing new dietary ingredients, firms are not required to disclose to the FDA or consumers the information they have about the safety or purported benefits of their dietary supplement products. Likewise, there is no prohibition against firms making this information available either to the FDA or to their consumers. It is up to each firm to set its own policy on disclosure of such information.

The FDA Center for Food Safety and Applied Nutrition is responsible for the agency's oversight of these products. The FDA's efforts to monitor the marketplace for potentially illegal products (products that may be unsafe or make false or misleading claims) include obtaining information from inspections of dietary supplement manufacturers and distributors, the Internet, consumer and trade complaints, occasional laboratory analyses of selected products and adverse events associated with the use of supplements that are reported to the agency.¹⁴

Labeling. FDA regulations require that certain information appear on dietary supplement labels including: a descriptive name of the product stating that it is a "supplement;" the name and place of business of the manufacturer, packer or

What Health Care Providers Can Do to Help Prevent Adverse Events

Because of the potential for herb-drug interactions and surgical complications, it is as important to be as aware of patient herbal usage as their prescription drug use. Carefully question patients about their histories and document it in the medical record. It is important to:

- Ask all patients about herbal therapy, dietary supplement or other natural substance use in person, using neutral language. Document use in the patient chart.
- Ask patients to bring herbal supplements with them to their visits. During questioning about herbal usage, one in five patients can't identify the preparation.
- Question patients about symptoms from undiagnosed conditions that may lead to disclosure of herbal usage.
- Be aware of the potential for contamination and variation among products.
- Avoid combining herbs and prescription medications due to the risk of potential interactions.
- Advise patients not to use larger than recommended doses.
- Advise patients not to use herbs if they plan to become pregnant or are pregnant or nursing.
- Advise patients to avoid long term use (more than several weeks).
- Tell patients that infants, children and geriatric patients should not be given herbs without the approval of a health care provider.
- Spend time developing and explaining patient-specific treatment plans. Patients who understand and are partners in their treatment are more likely to be compliant. Many patients solicit alternative practitioners because they view them as having beliefs consistent with their own and these practitioners often spend more time talking and listening to them.
- Take time to study alternative therapies so you are knowledgeable and can educate your patients. Knowledge is an important part of patient safety.
- Document any adverse events in the patient chart and report them to the FDA MedWatch program.^{6,7,12,17}

distributor; a complete list of ingredients; and the net contents of the product. In addition, each dietary supplement (except for some small volume products or those produced by eligible small businesses) must have nutrition labeling in the form of a "Supplement Facts" panel. This label must identify each dietary ingredient contained in the product. Ingredients not listed on the "Supplement Facts" panel must be listed in the "Other Ingredient" statement beneath the panel.¹⁴ Ingredient labeling must include the name and quantity of each dietary ingredient or, for proprietary blends, the total quantity of all dietary ingredients (excluding their inert ingredients) in the blend. Labeling of products containing herbal and botanical ingredients must state the part of the plant from which the ingredient is derived. If a supplement is covered by specifications in an official compendium and is represented as

conforming, it is misbranded if it does not conform to those specifications. Official compendia include the US Pharmacopeia, the Homeopathic Pharmacopeia of the United States or the National Formulary. If not covered by a compendium, a dietary supplement must be the product identified on the label and have the strength it is represented as having.¹⁵

A product sold as a dietary supplement and promoted on its label or in labeling as a treatment, prevention or cure for a specific disease or condition would be considered an unapproved and thus illegal drug. By law, manufacturers may make three types of claims for their dietary supplement products: health claims, structure/function claims and nutrient content claims.¹⁴

Adverse Event Reporting. The MedWatch program provides a way for health care providers to report problems believed to be caused by FDA-regulated



products such as drugs, medical devices, medical foods and dietary supplements. Health care providers can call FDA's MedWatch hotline at 1-800-FDA-1088, submit a Medwatch reporting form by fax to 1-800-FDA-0178 or on-line at <http://www.fda.gov/medwatch/report/hcp.htm>. Consumers can also make reports directly to the FDA.¹⁴ Identities of patients are kept confidential.¹⁶

Acknowledgment

The North American Spine Society Patient Safety Task Force would like to acknowledge Elizabeth Aronsen, MD, and Lisa Winslow, MD, for their contribution of *Herbs With Potential Adverse Effects for Surgical Patients* to this publication. This document provided the basis for development of this publication and provided much of the unreferenced material.

Endnotes

1. Paracelsus PA. The Speaker's Electronic Reference Collection." Aapex Software. 1994.
2. Wetzel MS, Eisenberg DM, Kaptchuk TJ. Course involving complementary and alternative medicine at US medical schools. *JAMA*. 1998;280:784-787. Cited by: Eisenberg DM, Davis RB, Ettner SL, et al. Trends in alternative medicine use in the United States, 1990-1997. Results of a follow-up national survey. *JAMA*. 280:1569-2575.
3. Pelletier KR, Marie A, Krasner M, et al. Current trends in the integration and reimbursement of complementary and alternative medicine by managed care, insurance carriers, and hospital providers. *Am J Health Promot*. 1997;12:112-122. Cited by: Eisenberg DM, Davis RB, Ettner SL, et al. Trends in alternative medicine use in the United States, 1990-1997. Results of a follow-up national survey. *JAMA*;280:1569-2575.
4. Eisenberg DM, Davis RB, Ettner SL, et al. Trends in alternative medicine use in the United States, 1990-1997. Results of a follow-up national survey. *JAMA*;280:1569-2575.
5. Spake A. Natural hazards. Tonic or toxic? Americans are gobbling up nature's remedies for everything from obesity to depression. *US News & World Report*. 2001;130(6):42-49.
6. Flanagan K. Preoperative assessment: safety considerations for patients taking herbal products. *Journal of PeriAnesthesia Nursing*. 2001;16(1):19-26.
7. Bullock K. Alternative therapies: helping patients find their way. *Focus on Patient Safety*. 1999;2(2):1-2.
8. Leung JM, Dzankic S, Manku K, Yuan S. The

Resources

- Trenter, ML (ed). US Food and Drug Administration Center for Drug Evaluation and Research-Special Report. From test tube to patient: improving health through human drugs. 1999. Available at: <http://www.fda.gov/cder>. Accessed June 4, 2002.
- US Food and Drug Administration Center for Drug Evaluation and Research. OTC drug monograph review process-review by CDER. Available at: <http://www.fda.gov/cder/handbook/otcrevw.htm>. Accessed June 4, 2002.
- US Food and Drug Administration Center for Drug Evaluation and Research. Over-the-counter drug products. Available at: <http://www.fda.gov/cder/handbook/otcintro.htm>. Accessed June 4, 2002.
- US Food and Drug Administration Center for Drug Evaluation and Research. Questions about CDER. Available at: <http://www.fda.gov/cder/about/faq/default/htm>. Accessed June 4, 2002.

Many of the following resources provide extended links to other information sources.

- American Academy of Orthopaedic Surgeons. CAM Herb/Drug Interactions. <http://www3.aaos.org/courses/cam/dhintact.htm>.
- American Society of Anesthesiologists. Considerations for Anesthesiologists: What You Should Know About Your Patients' Use of Herbal Medicines. <http://www.asahq.org/ProfInfo/herb/herbbro.html>.
- National Center for Complementary and Alternative Medicine, National Institutes of Health. Provides links for consumers and health care providers including fact sheets, alerts and advisories, consensus reports, databases, etc. <http://www.nccam.nih.gov/index.html>.
- US Food and Drug Administration Center for Food Safety and Applied Nutrition. Provides an overview of dietary supplements including links to warnings and safety information, adverse event reporting, general information, industry information and regulations, frequently asked questions and other sources of information. <http://www.cfsan.fda.gov/~dms/supplmnt.html>.
- The US Pharmacopeia. Provides a section on dietary supplements discussing USP programs and provides informational monographs. <http://www.usp.org>.

prevalence and predictors of the use of alternative medicine in presurgical patients in five California hospitals. *Anesthesia and Analgesia*. 2001;93(4).

9. AMA Council on Scientific Affairs. Report 13 (A-97). Folk remedies among ethnic subgroups (revision). Available at: <http://www.ama-assn.org/ama/pub/article/2036-2524.html>. Accessed December 20, 2001.
10. Blendon RJ, DesRoches CM, Benson JM, Brodie M, Altman DE. American's views on the use and regulation of dietary supplements. *Arch Intern Med*. 2001;161:805-810. Cited by: Ang-Lee MK, Moss J, Yuan CS. Herbal medicines and perioperative care. *JAMA*. 2001;286:208-216.
11. Elder NC, Gillcrist A, Minz R. Use of alternative health care by family practice patients. *Arch Intern Med*. 1997;6:181-184. Cited by: Ang-Lee MK, Moss J, Yuan CS. Herbal medicines and perioperative care. *JAMA*. 2001;286:208-216.
12. Ang-Lee MK, Moss J, Yuan C-S. Herbal medicines and perioperative care. *JAMA*. 2001;286:208-216.
13. US Food and Drug Administration Center for Food Safety and Applied Nutrition. Dietary

supplements. Overview. Available at: <http://www.cfsan.fda.gov/~dms/supplmnt.html>. Accessed February 27, 2002.

14. US Food and Drug Administration Center for Food Safety and Applied Nutrition. Overview of dietary supplements. January 3, 2001. Available at: <http://www.cfsan.fda.gov/~dms/ds-oview.html>. Accessed February 27, 2002.
15. US Food and Drug Administration Center for Food Safety and Applied Nutrition. Dietary supplement health and education act of 1994. December 1, 1995. Available at: <http://www.cfsan.fda.gov/~dma/dietsupp.html>. Accessed February 27, 2002.
16. US Food and Drug Administration Center for Food Safety and Applied Nutrition. Adverse event reporting. December 6, 2001. Available at: <http://cfsan.gda.gov/~dms/ds-rept.html>. Accessed February 27, 2002.
17. Kassler WJ, Blanc P, Greenblatt R. The use of medicinal herbs by human immuno-deficiency virus-infected patients. *Arch Intern Med*. 1991;151:2281-2288. Cited in: Ang-Lee MK, Moss J, Yuan C-S. Herbal medicines and perioperative care. *JAMA*. 2001;286:208-216.