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HERBALGRAM

The Journal of the American Botanical Council

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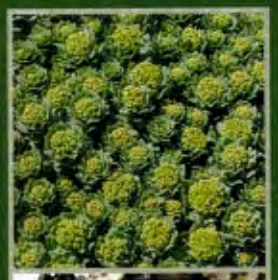
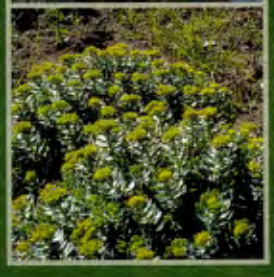


Rhodiola Rosea

A Phytomedicinal Overview



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ABC continues to develop and distribute educational literature to advance the field of phytomedicine. As an independent research organization, ABC publishes health and therapeutic information on herbs in its literature. A complete range of booklets, pamphlets and reports are published and distributed worldwide to students, educators, healthcare providers, and researchers. Your membership dollars help us provide this information.

Educational and Research Initiatives

The ABC Education Department administers an active internship program for students of pharmacy and dietetics. The department initiates research projects and is available to answer questions from members, the media and industry representatives.

Your membership in the American Botanical Council and contributions to our efforts make our work possible.

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In 1998, ABC acquired an historic 2.5 acre site originally known as the Case Mill Homestead. The property encompasses a 150-year-old main building, educational facilities, materials inventory building, greenhouse, rainwater collection system, and 15 medicinal theme gardens. Healthcare professionals and visitors from all over the world attend seminars and tour these facilities that are maintained through your membership contributions. Planned expansion will be possible through additional funding.

Health Professional Education Projects

ABC is involved in providing continuing education opportunities for health professionals. Projects are produced by ABC in conjunction with the accrediting agencies in each health profession. In addition to continuing education modules, ABC sponsors ethnobotanical tours that offer

credit for courses set in the rainforests of Africa and Peru. Such tours further the understanding of the importance of preserving indigenous cultures and plants throughout the world.

The latest CE book, *The ABC Clinical Guide to Herbs*, consists of comprehensive monographs on widely used herbs, plus a clinical overview, a patient information sheet, table of clinical studies listing brands tested for each herb, and other unique features.

Membership Levels

Individual – Benefits include membership card, one year subscription to *HerbalGram*, free herbal medicine book, access to password protected areas of the ABC website, including *HerbalGram* archives, discounts on merchandise from the Herbal Education Catalog, free initial research session with our education department (up to 20 minutes) and 40% discount on additional research. **$50 annually**, discounts for seniors and students available.

Academic – All benefits above, plus online access to: HerbClip Online, full line of booklets and pamphlets, continuing education materials, and other protected areas of the ABC website. **$100 annually**

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For Corporate and Sponsor Member donation levels, please contact Wayne Silverman, PhD at wsilverman@herbalgram.org or 512/926-4900 ext 120.

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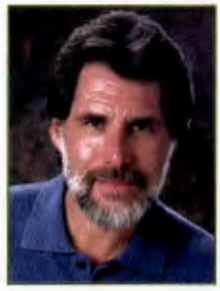
(continues)

dear reader

Go to war with Iraq? There seems to be another undeclared war, the war on herbs. Here's a summary of recent "news from the front-lines."

St. John's wort. In April the *Journal of the American Medical Association* published the results of the NIH's first trial on St. John's wort, concluding that neither SJW nor the prescription drug Zoloft® were more effective than placebo *in this particular trial.* Media coverage fixed almost solely on SJW, with consumers getting the erroneous message that it "doesn't work." Jerry Cott, Ph.D., comments on the study in this issue of *HerbalGram.*



PC-SPES. In a situation that justifiably raised concerns across the board, BotanicLab, marketer of the controversial supplement PC-SPES, ceased operations in June, citing its inability to obtain uncontaminated product from Chinese suppliers. In February the FDA ordered the recall of SPES (an immunostimulant herb combination) and PC-SPES (made from seven Chinese herbs plus saw palmetto, shown in published clinical trials to treat prostate cancer). The California Department of Health Services' Food and Drug Branch found the prescription drugs alprazolam in SPES and warfarin (Coumadin®) in PC SPES. An NIH-funded trial on PC-SPES at Johns Hopkins was halted due to the revelations of the adulteration. Tragic is the inability of thousands of prostate cancer patients to obtain it, since they, and many urologists and oncologists, believed it produced benefits when there were few viable alternatives (visit <www.herbalgram.org>).

Kava. The German government surprised everyone in June, revoking licenses for kava drugs effective immediately. The action followed reports associating kava with hepatotoxicity, even though many cases include other confounding factors that make direct causal links between kava and liver toxicity uncertain. The vaunted German Commission E had recommended that kava remain on the market as a prescription drug. Other countries followed Germany's lead, with removal in Singapore, a voluntary withdrawal in Australia, and a ban and recall in Canada. Kava was our last issue's cover story. For new information, see the ABC website <www.herbalgram.org/browse.php?content_name=kavaupdate2>.

Institute of Medicine Safety Report. In July the National Academy of Science's Institute of Medicine released a 156-page draft report on its framework to evaluate the safety of dietary supplements. This may be adopted by FDA to help establish a (hopefully) rational system to determine safety of popular supplement ingredients (more at <www.iom.edu>). IOM identified six supplements for which it was drafting safety reviews including two herbs: chaparral and saw palmetto (SP). Some cases of hepatotoxicity were associated with chaparral in 1993 (see article in *HerbalGram* 28). Chaparral has little market presence today; a safety review of kava might have been a better investment of IOM resources. SP is on the list because FDA has two case reports of cardiac incidents associated with SP consumption, although causality has not been established. IOM added SP to its safety review process, with the predictable outcome of a clean bill of health, as it assuredly

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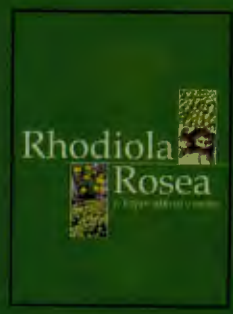
Departments



On the cover

Rhodiola rosea
Background image: Lamarck, Jean Baptiste Pierre Antoine Monet de. *Encyclopédie méthodique* ... Paris, 1782-1823 – plate 819, bottom half of page. Courtesy of The Hunt Institute for Botanical Documentation.

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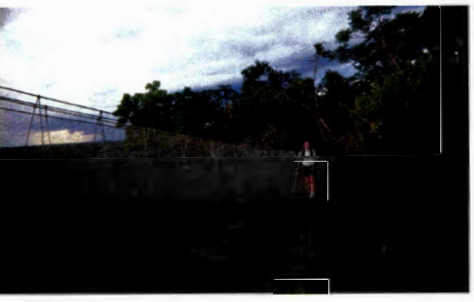
Features

Rhodiola rosea Sowerby, James. *English botany; or, coloured figures of British plants* .... London, Printed for the author, by J. Davis, 1790-[1814]. -- vol. 8, plate 508 Courtesy of The Hunt Institute for Botanical Documentation.

ABC Partners with HealthQuest, Offers Members New Benefit

The American Botanical Council is pleased to announce a new partnership with HealthQuest Travel and Education. After eight years of coordinating ethnobotanical tours for International Expeditions, Charlotte "Chuck" de Frances partnered with Mindbodytravel.com to form HealthQuest and expand the scope of destinations and programs of the healthcare travel series she inaugurated. This, in turn, has provided a new opportunity for ABC. Having co-sponsored the healthcare travel series since its beginning, ABC is happy to continue its relationship with Chuck and is excited about the possibility of an expanded series of tours.

As part of its partnership with HealthQuest, ABC is now able to offer a new membership benefit — a discount on the cost of the tours. Members who join at the Individual level ($50) receive a $50 discount on any of the trips. Academic members ($100) receive a $100 discount. Members at the Professional level and above ($150 and up) may deduct $150 from the cost of any of the healthcare series tours. All they need to do is enter their ABC member number on the registration form and the discount will be applied.



The ACEER canopy walkway above the Amazon rainforest, one of the exciting educational destinations of ABC's ethnobotanical tours. ©2002 Trey Bennett

For more information on ethnobotanical tours, visit <www.herbalgram.org/browse.php/ed_tours> or call Stacy Elliott at 800/373-7105 ext. 101. For more information about membership, visit <www.herbalgram.org/browse.php/membership> or call Kim West at 800/373-7105 ext. 119.

Upcoming tours include:

Belize and Tikal: Perspectives in Healthcare – 11/30-12/7, 2002

Amazon: Pharmacy from the Rainforest – 2/1-2/9, 2003 (6-day extension to the Andes and Machu Picchu)

Southern Africa Safari (Kalahari Desert/Okavango Delta) – 8/1-8/14, 2003 (3-day extension to Cape Town and 3-day extension to Victoria Falls)

China and Yangtze River Voyage – 9/7-9/21, 2003

Attention ABC Members

Please provide us with your email address if you want to receive periodic updates concerning breaking news in the herbal community. Email to kwest@herbalgram.org.

Dear Reader

Continued from page 4

deserves. But minor damage was done; SP was reported along with the other ingredients as "controversial supplements," possibly raising unwarranted concerns among wary consumers.

Ephedra. Many industry insiders have feared that ephedra may become the Achilles' heel of herbs. Its potential risks draw increasing attention from health professionals, regulators, and media. Insiders say, "If we could just get ephedra off the table, we could focus on other herbs whose safety and benefits are not so controversial."

But ephedra seems to *be* the table with numerous professional groups lining up against it. In July U.S. Sen. Dick Durbin (D-IL), who chaired a hearing on weight-loss supplements, called on HHS Secretary Tommy Thompson to determine immediately whether ephedra supplements pose an "imminent hazard" to public health, and if so, to suspend sales. In mid-August FDA and the Justice Department initiated a criminal investigation of Metabolife International, a leading manufacturer of dietary supplements containing ephedra, for allegedly making false statements to the government. The company voluntarily made available more than 14,700 consumer call records (the majority of which are minor events). Over the last five years, more than 4.5 billion tablets and 50 million bottles of Metabolife 356 have been sold, according to a company letter to Thompson. About 78 of the reports appear to be serious incidents, including hospitalizations and reportedly one death. Most of the incidents are reportedly consistent with the occurrence of these conditions in the general population, according to experts who have reviewed them. Media accounts imply that all 14,700 "incident reports" were "serious" — clearly, a gross exaggeration.

It is not clear, however, whether the new disclosures are included in previously published adverse events associated with ephedra. The consensus of many experts, including the GAO and the FDA, however, is that AERs are not a valid scientific basis upon which to develop regulatory policy on the safety of a substance. In July FDA asked industry members whether they support mandatory reporting of all ephedra AERs. Metabolife said "yes," although industry groups have not yet responded. Will Congress and FDA combine the ephedra and PC-SPES issues to call for tighter regulation of *all* herbs? These herbs generate so much "heat," others may get swept up in the furor.

Ginkgo. With so many problems being reported (and misreported), some herbs have so much accumulated research, they should be relatively immune from bad press (e.g., ginkgo). But no. As if things weren't bad enough, *JAMA* published and heavily promoted a study that failed to show positive effects of ginkgo on memory and concentration in healthy older adults (60 years plus). AMA distributed video news releases (via satellite) to TV stations. Coverage on the *CBS Evening News with Dan Rather* suggested that consumers should not buy ginkgo. As pointed out in ABC's press release, which is available online at <www.herbalgram.org/browse.php/081902press>, one study does not invalidate the impressive research record for the cognitive benefits for ginkgo extract. We emphasized that another recent study on ginkgo following a similar design for the same period of time (6 weeks) on a similar population of healthy adults produced positive effects, at a dosage of only 50 percent more (180mg per day). This was virtu-

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Aristolochic Acid Evaluation Program: Standards of Identity for the Responsible Trade of Chinese Medicinal Herbs

The American Herbal Pharmacopoeia (AHP), in collaboration with the American Herbal Products Association, the Therapeutic Goods Agency of Australia, and the State Drug Administration of China, is establishing international standards for the identification of those plants known to contain aristolochic acid (AA) and those that may become adulterated with AA-containing plants.

In recent years, Chinese herbal formulas containing AA have been associated with numerous case reports of kidney failure and kidney cancer. Many of these adulterations are quite common and have led to import alerts and trade restrictions in several countries.

The aristolochic acid project is designed to protect and promote the responsible trade of Chinese medicinal herbs, specifically many of those cited by the U.S. Food and Drug Administration (FDA) as those that contain, or may be adulterated with AA-containing plants. These herbs include:

- stephania (*Stephania tetrandra* S. Moore, Menispermaceae),
- aristolochia (*Aristolochia fangchi* Y.C. Wu ex L.D. Chou & S.M. Hwang, Aristolochiaceae),
- costus (*Saussurea costus* (Falc.) Lipsch, Asteraceae, syn. *S. lappa* (Decne.) C.B. Clarke),
- Chinese wild ginger (*Asarum heterotropoides* F. Schmidt var. *mandshuricum* (Maxim.) Kitag, and *A. sieboldii* Miq., Aristolochiaceae),
- akebia (*Akebia quinata* (Houtt.) Decne., and *A. trifoliata* (Thunb.) Koidz., Lardizabalaceae)
- Armand's clematis (*Clematis armandii* Franch., Ranunculaceae)
- Chinese clematis (*C. chinensis* Retz., Ranunculaceae).

The primary goal of the Aristolochic Acid Evaluation Program is to develop standards from botanically verified samples that have already been obtained, to develop multiple validated methods of identification (macroscopic, microscopic, and thin-layer chromatography fingerprinting), and to combine this with analytical work currently underway by FDA in validating analytical methods for the analysis of AA. This will then be formally presented to herbal products manufacturers and regulatory agencies worldwide as the definitive body of information needed to identify these botanicals, thereby taking the self-regulatory steps needed to protect public health. The program will also provide recommendations for the appropriate trade or restriction of these botanicals.

Seed money to help offset the cost of obtaining authenticated botanical voucher samples was provided by the Chinese Herbal Products Committee of the American Herbal Products Association through contributions from Golden Flower, Health Concerns, Chuanheng Management, KPC Products, Inc., K'an Herb Co., and Crane Herb Co. Contributors will receive a complimentary copy upon completion.

Further funding is needed. To support the Aristolochic Acid Program and receive the future publication of the Aristolochic Acid Evaluation Program: Standards of Identity Document, contact the AHP.

For more information, contact: AHP's executive director, Roy Upton at P.O. Box 66809, Scotts Valley, CA 95067, USA, Tel: 831/461-6317, Fax: 831/475-6219, or email: <herbal@got.net>.

[American Herbal Pharmacopoeia. Aristolochic Acid Evaluation Program: Standards of Identity for the Responsible Trade of Chinese Medicinal Herbs (press release). 2001 June 13.]

AHPA Extends Product Label Recommendation to Class 3 Botanicals

The American Herbal Products Association (AHPA) recently expanded its Trade Recommendation about safety labeling to include Class 3 botanicals. Class 3 botanicals are those that pose significant health risks as defined by AHPA's *Botanical Safety Handbook*.

AHPA previously evaluated herbs sold in the U.S. marketplace and placed them into four classes:

Class 1: herbs which can be safely consumed when used appropriately;

Class 2: Herbs with use restrictions:

2a: external use only;

2b: contraindicated during pregnancy;

2c: contraindicated during lactation;

2d: Other contraindications (e.g., hypertension, diabetes, etc.);

Class 3: herbs that should be used only under the supervision of a qualified expert;

Class 4: herbs that cannot be classified because of insufficient information.

The *Botanical Safety Handbook* (1997) lists about 550 herbs in trade and their classifications. The handbook also provides specific cautionary language to be included on product labels.

Formerly, only products in Class 2b or 2c had labeling requirements under AHPA policy. Membership in AHPA is contingent upon meeting these standards, among others.

Effective October 2003, product labels on Class 3 herb should include the following label information: "To be used only under the supervision of an expert qualified in the appropriate use of this substance."

Product labels on Class 3 herbal ingredients must also include: proper use information, dosage, contraindications, potential adverse effects and drug interactions, and any other relevant information related to the safe use of the substance. In addition, products containing Class 3 herbal ingredients must be labeled "not for general retail sale" and should be marketed so as to prevent general retail sale.

If the manufacturing process sets aside the safety concern, a product that contains a Class 3 herb need not include the recommended label information.

Two examples of Class 3 herbs are belladonna or deadly nightshade (*Atropa belladonna* L., Solanaceae), mayapple or American mandrake (*Podophyllum peltatum* L., Berberidaceae).

The entire list of Class 3 herbs can be found on page 189 of *The Botanical Safety Handbook*, which is sold by the American Botanical Council (ABC catalog #B275) and AHPA.

[AHPA. Update New AHPA Trade Recommendation [press release]. 2002 April 23.]

White House Commission on Complementary and Alternative Medicine Policy Issues Final Report

by Hannah V. Bradford, M.Ac., L.Ac., MBA

The eagerly anticipated Final Report of the White House Commission on Complementary and Alternative Medicine Policy (WHCCAMP) was released in March 2002, and is now available on the Commission's website <www.whccamp.hhs.gov>.*

Formally received by Secretary of Health and Human Services (HHS) Tommy G. Thompson, the Final Report is currently under review by his agency and others. Various groups representing practitioners, educators, and complementary and alternative medicine (CAM) product manufacturers have distributed position statements and have met with Administration officials and journalists in attempts to shape the eventual White House response.

Key Proposed Actions of the Commission

The WHCCAMP Final Report lists 29 recommendations and 105 actions, organized around the topics of research, education and training, information development and dissemination, access and delivery, and coverage and reimbursement. The most significant recommendations are:

- Create a CAM office at the highest level with the Department of Health and Human Services.
- Develop research infrastructure at CAM institutions.
- Create demonstration projects of residencies and postgraduate training for appropriately educated and trained CAM practitioners.
- States should, as appropriate, implement provisions for licensure, registration, and exemption consistent with the practitioners' education, training, and scope of practice.
- Develop analytical methods for producing better CAM products.
- Increase CAM-conventional collaborative research projects.
- Explore expansion of loan programs to students at CAM institutions.
- Support federal research on CAM cost-effectiveness and cost-benefit analysis.
- Require periodic reports from federal agencies on CAM benefit policy and their inclusion of CAM experts on advisory boards.

Other recommendations of potential interest to the herbal communities include:

- Increase U.S. Food and Drug Administration (FDA) resources to fully implement the Dietary Supplement Health and Education Act of 1994 and in particular, finalize Good Manufacturing Practices, and simplify and expand the adverse events reporting system.
- Accelerate public and private efforts to develop validation and analytical methods and reference materials.
- Create an independent expert panel to develop an objective process for evaluating the safety of dietary supplements. This has been started by the Institute of Medicine's (IOM).
- Expand package insert information on dietary supplements, including risks, interactions, and benefits.
- Increase financial support to the Federal Trade Commission to identify deceptive advertising practices by dietary supplement manufacturers and develop consumer education programs.
- Institute voluntary registration of dietary supplement manufacturers with the FDA to facilitate notification of serious adverse events.
- Require manufacturer maintenance of records and reporting of serious adverse events to the FDA.

As stated by Joseph Pizzorno, N.D., a Commission member and long-time naturopathic educator and practitioner, the most significant aspect of the Commission is "that it actually happened."

The release of the Final Report calls on all CAM groups, practitioners, manufacturers, and consumers, to "take themselves and the issues more seriously since now all levels of the culture are paying attention to these issues," Pizzorno said. "If we build on the groundwork laid by the Commission and support implementation of the key recommendations, we can substantially level the playing field of healthcare services."

For the herbal community, the Commission's recommendations require development of clear statements of product quality and lend encouragement to herbal practitioners to develop their own standards of practice and credentialing.

Other recommendations of importance fall in the areas of Research, Education and Training, Information Development and Dissemination, Access and Delivery, and Coverage and Reimbursement. Highlights in these areas are:

Research

The Report calls for significantly more research support for CAM, with emphasis on the following:

- Federal research support for practices and products that may be effective, but not profitable to, nor patentable by private investors.
- Creation of outreach programs to inform manufacturers about federal research support available to private industry.
- Creation of language by state professional regulatory bodies to protect practitioners of CAM engaged in research from sanctions.
- Expansion of the Agency for Health Care Research and Quality's Evidence-based Practice Center review of CAM.

Education and Training

The general tenor of the education and training section remained the same as in the Interim Report (released September 18, 2001). The primary shift was the substitution of "feasibility studies" for "demonstration projects" in the areas of loan forgiveness for students and the addition of CAM practitioners to primary care teams. This change may lower the priority of the action, but increases leeway to policymakers in acting on these recommendations. A clear intent is to foster relationships between CAM and conventional education and training programs, with a recommendation to increase the core curriculum of each other's practices and concepts. Federal support, in conjunction with professional organizations, was recommended to develop education and training guidelines. (See education and training recommendations in above "Key Proposed Actions of the Commission.")

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* Within the next few months, the Commission's printed report will be made available to all interested parties. *HerbalGram* will publish ordering information in *HerbalGram* 57.

Information Development and Dissemination

This section addresses several key concerns that have implications for other areas, especially education, research, and access and delivery. A central recommendation is for the Secretary of HHS to set up a Task Force to identify and eliminate existing CAM information gaps throughout the entire Federal government. More specific actions recommended in this section include:

- Relevant federal agencies should create easy-to-understand public information materials on CAM.
- Expand the National Library of Medicine and American Library Association training programs for librarians to help consumers access CAM information.
- Create a public-private partnership to develop standards for website information on CAM.
- Request that States require disclosure of practitioners' level of training, scope of practice, licensure, certification, and disciplinary actions.

Access and Delivery

Access and delivery policy issues are likely to be a central focus of the proposed new federal office on CAM. Recommended actions include:

- Provide federal assistance to the States in evaluating the impact of CAM legislation and developing regulation and oversight of CAM services and products.
- Identify national healthcare needs, and analyze the relevance of CAM services.
- Create a policy advisory committee to address access to CAM practitioners and to foster collaboration among CAM organizations on consensus for standards of practice and education and training.
- Assist evaluation by accrediting bodies of conventional healthcare organizations of their CAM policies.
- One recommendation and three related actions were proposed to address special and vulnerable populations, including demonstration projects that integrate CAM services into existing delivery models.

Coverage and Reimbursement

Several actions proposed in this section require funding of health services research on CAM cost-effectiveness and cost-benefits. A national coding system for CAM and periodic reports from federal agencies on coverage and reimbursement policy would further support inclusion of CAM in benefit programs. Proposals to encourage federal agencies to develop appropriate clinical criteria for CAM services in their programs and add CAM experts to relevant advisory committees were detailed. Other recommendations include:

- Demonstration projects to analyze how CAM may contribute to addressing the 10 leading indicators of health.
- Adding CAM practices questions to national surveys.
- Public information campaigns on nutrition, exercise, and stress management CAM practices.
- Incentives to schools to make healthy snacks and lunches and to eliminate advertising of products such as high-fat snacks and soft drinks.
- Evaluate the role of CAM practices and products in workplace wellness and prevention activities and create incentives to develop the resultant programs.
- Inclusion of self-care and lifestyle decision-making curriculum in professional CAM and conventional training programs.

The CAM Office

A proposed office to coordinate federal efforts was envisioned as the mechanism to implement the Commission's recommendations and other, emerging issues in CAM. The specifics include:

- An office at the highest possible and most appropriate level in the Department of Health and Human Services.
- An advisory committee with conventional and CAM experts, and representatives of the public and private sectors.
- The office's responsibilities would include coordinating the federal effort in CAM; convening conferences and workshops; acting as the primary point of contact on CAM with the public, practitioners, and the media; and exploring additional topics not covered by the Commission.

Early Effects of the Report

The following major activities were at least partially motivated by release of Final Report of the Commission:

- The National Policy Dialogue Report, sponsored by a coalition of CAM groups, was delivered to members of Congress. This report expands and clarifies the central recommendations of the Commission. Since May 2002, various representatives of the Dialogue's sponsoring groups have met with Congressional staff, senators, and representatives to discuss specific initiatives.
- Several members of Congress have launched a serious evaluation of CAM issues. The Complementary and Alternative Medicine and Natural Foods Caucus was formed by Senators Tom Harkin (D-IA) and Orrin G. Hatch (R-UT) and Representatives Dan Burton (R-IN) and Dennis Kucinich (D-OH).
- Perhaps more significantly, in anticipation of the Commission's report, the Congressional Appropriations Conference Committee Report urged "the Secretary [of HHS] to form a coordinating unit to review the Commission's report and implement ways to better coordinate the Department's many CAM-related activities." The full text of the committee report is available through <www.thomas.loc.gov> under "Status of 2002 Appropriations Bills."
- During the life of the WHCCAMP, the IOM acted on a key Commission recommendation to set research priorities by developing its "Proposed Framework for Evaluating the Safety of Dietary Supplements," the goal of which is the establishment of direction in the study of dietary supplements. The 156-page report was released in July 2002, and is open for comments. It is available online only at the National Academy Press website, <www.nap.edu/catalog/10456.html>.

Clearly, the delivery of the Final Report of the White House Commission on CAM Policy represents a historic shift in healthcare policy in this country. The clear thinking and serious deliberation brought to this effort by the Commission staff and members, it is hoped, will inspire the entire CAM community to take up its role in shaping future policy.

Hannah V. Bradford, is a licensed acupuncturist in Bethesda, Maryland and publishes CAM Communications and Reports. Information at: <hvbradford@cs.com>.

WHO Publishes Traditional Medicine Strategy for 2002-2005

The World Health Organization (WHO) has announced the development of a strategy to increase the number of member nations having a national policy and legal framework to deal with complementary and alternative medicine (CAM), particularly the growing use and distribution of botanical medicines.

The report, titled *WHO Traditional Medicine Strategy 2002-2005,* was presented May 16 at the World Health Assembly in Switzerland. This report is heavily focused on botanicals and the need to establish regulation of herbal products. Consistent with its previous positions and publications in this area in the past decade, WHO acknowledges the significant role that herbal preparations can offer as low-cost medicines when they are properly manufactured and rationally evaluated for their safety and efficacy.

The 74-page report indicates an intention to bring "order" to the practice and use of traditional medicines, which mainly refers to botanicals and other natural products used medicinally in systems of indigenous and traditional medicine.

The Traditional Medicines Strategy identified the following "key needs":

- National regulation and registration of herbal medicines.
- Post-marketing surveillance of herbals to monitor safety.
- Support of clinical research on the use of CAM for common health problems; these include the use of traditional medicines in the areas of infectious diseases, as they may be appropriate, as well as the growing problems with AIDS in many developing countries.
- Creation of national monographs for medicinal plants (many of these would presumably follow the outline and work already being done on the monographs being published by WHO).

WHO had previously published "Guidelines for the Assessment of Herbal Medicine" in 1991. (See *HerbalGram* 28, pp. 13-20 for complete text.) In addition, WHO has published a volume of herbal monographs to establish guidelines for identity, quality, safety and effective use, *WHO monographs on selected medicinal plants Volume 1* (WHO, 1999; see "Monograph Update" article in *HerbalGram* 47, pp. 40-45, for a table showing the uses of medicinal plants supported by clinical data in WHO monographs).

The complete text of the *WHO Traditional Medicine Strategy 2002-2005* is available online at <www.who.int/medicines/organization/trm/orgtrmmain.shtml>.

—Mark Blumenthal

USP's Dietary Supplement Verification Program Unveils Mark

The United States Pharmacopeia (USP) created its Dietary Supplement Verification Program (DSVP) in November 2001 to help inform and safeguard the growing number of consumers who use dietary supplements. USP recently unveiled the mark that qualifying manufacturers will place on their product labels.

Nature Made® Vitamin E was the first product to earn the DSVP mark. Nature Made is a division of Pharmavite LLC, of Northridge, CA, one of the nation's largest dietary supplement manufacturers. Pharmavite was the first company to join DSVP. Leiner Health Products Inc. of Carson, CA; Inverness Medical Innovations Inc. of Waltham, MA; and Weider Nutrition International Inc. of Salt Lake City, UT, are also participating in DSVP.

Under DSVP, USP evaluates and verifies dietary supplements according to stringent standards for product purity, accuracy of ingredient labeling, and proper manufacturing practices. The DSVP mark helps assure consumers, health care professionals, and supplement retailers that a product:

- Contains the ingredients declared on the product label;
- Contains the amount or strength of ingredients declared on the product label;
- Meets requirements for limits on potential contaminants
- Has been manufactured properly by complying with USP and proposed FDA standards for good manufacturing practices (GMPs).

Once a dietary supplement is granted the USP DSVP certification mark, USP will periodically conduct random off-the-shelf tests on verified products to ensure they continue to meet DSVP's strict standards. USP also will continue to conduct audits of manufacturer sites for GMP compliance on a three-year basis. During the intervening years, manufacturers will be required to conduct annual self-audits and report the results to USP for review.

USP evaluates dietary supplements submitted to the program based on:

- Extensive laboratory testing;
- Comprehensive review of quality control and manufacturing documentation; and
- Evaluation of manufacturer compliance with USP and proposed FDA standards for GMPs.

USP is a not-for-profit organization that achieves its goals through the contributions of volunteers representing pharmacy, medicine, and other healthcare professions, as well as science, academia, government, the pharmaceutical industry, and consumer organizations.

Since 1820, USP has established standards for more than 3,800 prescription and over-the-counter medicines. USP also has developed monograph standards for more than 900 nutritional and dietary supplement products. These standards are compiled in the *United States Pharmacopeia* and *National Formulary* (*USP–NF*), which is recognized as the nation's official compendia for pharmaceuticals and dietary supplements. For further information, visit the DSVP website, <www.usp-dsvp.org>.

—Karen Robin

[USP. Nature Made Vitamin E Is First Dietary Supplement to Gain DSVP Certification (press release). 2002 June 17.]


NEW PATENT ON
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Scientifically Smart...Pycnogenol®
Pycnogenol®
French maritime pine bark extract
Nature's Super-Antioxidant — Pycnogenol® brand French maritime pine bark extract exclusively supplied in North America by Natural Health Science
Extensively researched for more than 30 years, Pycnogenol® helps to improve circulation, eye health, skincare, cardiovascular ailments, anti-aging, immunology and sports & endurance* And that's not all, for a complete list of scientific research and further information on Pycnogenol® please contact: Natural Health Science LLC
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Professor Sir Ghillean T. Prance Is 2002 Distinguished Economic Botanist

by Brian Boom, Ph.D.

Each year, the Society for Economic Botany (SEB), an international organization concerned with the relationships between plants and people, presents its Distinguished Economic Botanist (DEB) Award to an individual who has made outstanding contributions to the discipline. The winner of this, the SEB's highest honor, for 2002 is Professor Sir Ghillean T. Prance.

Prance

Over the years Professor Prance's career has been divided into several tracks, which he has remarkably managed to pursue simultaneously with excellence. He has been an administrator at several institutions, and is best known perhaps for his service as Senior Vice President for Science at the New York Botanical Garden (NYBG) and subsequently, as Director of the Royal Botanic Gardens, Kew in London. His administrative talents are currently being put to good use as Scientific Director of the Eden Project, based in Cornwall, England. The Eden Project brings the stories of our world to life in huge covered conservatories, or Biomes, that feature the majestic rainforests, the Mediterranean, South Africa, and California. The Eden Project's website is <www.edenproject.com>.

As a systematic botanist, Prance is best known for his monographic research on various tropical tree families, most notably the Brazil nut family (Lecythidaceae) and the Coco plum family (Chrysobalanaceae), and for his floristic studies of the Amazon. The Amazon, particularly the Brazilian Amazon, captivated most of his intellect and energies, and he established his credentials there as an economic botanist, having conducted ethnobotanical investigations with numerous indigenous groups. While at the NYBG, he founded and served as the first director of the Institute of Economic Botany, a department of the NYBG that continues to thrive today under the direction of Michael J. Balick, Ph.D.

In addition to his role with the Eden Project, Prance holds appointments at Reading University in England and at the National Tropical Botanical Garden in Hawaii. He is the author of 17 books and more than 400 scientific and popular papers in the fields of systematics, conservation, ecology, and economic botany. He holds 14 honorary degrees and is the recipient of numerous awards, such as the International COSMOS Prize (1993) and the Victoria Medal of Honour (1999). He was knighted in 1995 and was made a Commander of the Order of the Southern Cross by the President of Brazil in 2000.

Professor Prance is a mentor and an inspiration to numerous students over the years, including the author of this note. He is also a tireless speaker for the cause of biodiversity conservation and an officer in many scientific societies, including the SEB, for which he served as President in 1996. For a full account of this remarkable man, I recommend the biography by Clive Langmead: *A Passion for Plants: from the Rainforests of Brazil to Kew Gardens: the Life and Vision of Ghillean Prance, Director of the Royal Botanic Gardens, Kew*, Second edition (London: Royal Botanic Gardens, 2001).

The SEB's Distinguished Economic Botanist Award for this year was presented at the annual meeting, June 22–27, 2002, at NYBG, where Professor Prance delivered the banquet address after receiving the DEB Award.

The roster of DEBs over the past quarter century is a veritable "Who's Who" of economic botany: Julia F. Morton (1978), Richard E. Schultes (1979), Thomas W. Whitaker (1980), William H. Talent (1981), William L. Brown (1982), Norman R. Farnsworth (1983), Charles B. Heiser (1984), Jack R. Harlan (1985), Efraim Hernandez Xolocotzi (1986), Charles M. Rick (1987), Oswald Tippo (1988), Jack L. Beal (1989), Herbert G. Baker (1990), N. W. Simmons (1991), Douglas Yen (1992), Mildred Matthias (1993), Walton C. Galinat (1994), Varro E. Tyler (1995), Jack Hawkes (1996), Carlos Ochoa (1997), Hugh H. Iltis (1998), S. K. Jain (1999), James A. Duke (2000), and Isabella Abbott (2001).

To learn about and to join the SEB , visit its website: <www.econbot.org>.

Brian Boom, Ph.D., is the current President of the Society for Economic Botany. He also is Associate Director for Research and Adjunct Senior Research Scientist at the Center for Environmental Research and Conservation (CERC) of Columbia University.

NSF Dietary Supplements GMP Certification Program Certifies Contract Manufacturers

NSF International has awarded Good Manufacturing Practices (GMP) Registrations to three dietary supplement manufacturers. The first GMP registration was awarded to Perrigo Company's vitamin and nutritional supplement facilities in Greenville, SC; followed by Arizona Nutritional Supplements, of Chandler, AZ; and Natural Alternatives International, of San Marcos, CA.

GMPs are guidelines that provide a system of processes, procedures, and documentation to assure the product produced has the identity, strength, composition, quality, and purity represented on the product label. The NSF GMPs are consistent with industry recommended GMPs submitted to the U.S. Food and Drug Administration (FDA) in 1997. Should the FDA publish a final rule for dietary supplements GMPs, the NSF GMP requirements will be modified, if necessary, to be consistent. Certified companies undergo periodic audits to maintain the registration. NSF accepts National Nutritional Foods Association GMP audits into the NSF GMP Contract Manufacturers Registration Program.

NSF International, a not-for-profit, non-governmental organization, is the leading global supplier of risk-management services in public health and safety. NSF is a World Health Organization Collaborating Centre for Food Safety and Drinking Water Safety and Treatment. Serving companies in more than 83 countries, NSF was founded in 1944 and is headquartered in Ann Arbor, MI.

—Karen Robin

[NSF International. NSF Awards one of its first GMP registrations to Perrigo (press release). 2002 April 2.]

Libby Harvey FitzGerald Receives Tech Industry Award

Libby Harvey FitzGerald, manager and co-founder of Alpha Laboratories, has received the prestigious 2002 Technology Industry Award for the *North Bay Business Journal* second annual "Women in Business: Leaders, Innovators, Visionaries."


Harvey FitzGerald

Awards were given in nine industry categories. Technology industry nominations included top executives in semiconductor and electronic manufacturing, software, engineering, analytical laboratory services, pharmaceutical, biotechnology, medical devices, telecommunications, and consulting. The North Bay includes three major counties north of San Francisco: Sonoma, Napa, and Marin.

Winners were chosen based on a wide range of factors, including the individual's leadership role in her company and business-related innovations, achievements, and vision. Also considered were the nominee's length of service, career achievements, accomplishments in the North Bay area, and community involvement.

Ms. FitzGerald represents the scientific interests of the dietary supplement industry on a national level by her active service on the Analytical Laboratories Committee (Chair), Standards Committee, and Education Committee of the American Herbal Products Association (AHPA). In addition, she has been an invited speaker at APHA, AOAC International, National Institutes of Health, and National Nutritional Foods Association conferences. In 1997 she initiated a national educational seminar series entitled "Botanicals: Let's Talk Science." She received the prestigious AHPA Volunteer Service Award in 1999.

Since Alpha Laboratories founding in 1982 in Petaluma, California, Ms. FitzGerald has worn many hats, including HPLC and GC chemist, business manager, sales and marketing director, president, and CEO). In 1999, Eurofins Scientific acquired Alpha Laboratories to be its center-of-excellence for herbal products and dietary supplements. Alpha specializes in the analytical chemistry of natural products, development of combination sample extraction/instrumental methods, and method validation for raw material and finished products of the dietary supplement and pharmaceutical industries.

—Karen Robin

[Alpha Laboratories. Technology Leader, Innovator, Visionary … (press release). 2002 July 17]

Herb Society of America Honors Many, Names Blumenthal as Honorary President

The Herb Society of America (HSA) recognized the work of several people at its June annual meeting in Hershey, Pennsylvania. Further, American Botanical Council's Founder and Executive Director Mark Blumenthal was named Honorary President for a two-year term.

In a May 2002 letter, incoming HSA president Arlene Kestner, Ph.D., wrote that the choice of Blumenthal for Honorary President "was based upon your leadership role and achievements in establishing the American Botanical Council as the leading nonprofit education and research organization to provide science-based information on the safe and effective use of medicinal plants and phytomedicines."

Blumenthal, who replaces outgoing Honorary President Arthur O. Tucker, Ph.D., of Delaware State University, accepted the role "on behalf of all the employees here at ABC, both current and those who have worked here over the last 14 years, as well as for the ABC Board of Trustees."

At the June annual meeting, HSA bestowed the following awards:

The Helen de Conway Little Medal of Honor, for outstanding contributions to HSA or the world of horticulture in general, to Caroline W. Amidon, past president of HSA.

The Nancy Putnam Howard Award for Excellence in Horticulture, to Rebecca H. Talbot, of HSA's Nashville Unit.


Blumenthal

The Gertrude B. Foster Award for Excellence in Herbal Literature, to Deni Bown, photographer, lecturer and author of more than 20 books, and past chairman of the British Herb Society.

Certificates of Achievement were bestowed upon Mary S. Cartwright, of HSA's Nashville Unit; Marie Garvey Fowler, of HSA's Arkansas Unit; and Richard Ober (deceased) of the Potomac Unit.

Certificates of Appreciation were presented to Elsie Quarterman, Ph.D., of the Nashville Unit for her rediscovery of *Echinacea tennesseensis* (Beadle) Small, Asteraceae, which was once thought to be extinct; to Rosa Schachle of the North and Central Texas Unit; and Dalmae Tucker, of the Baton Rouge Unit.

Based in Kirtland, Ohio, the HSA was founded in 1933, and is dedicated to promoting the knowledge, use, and delight of herbs through educational programs, research, and sharing the experience of its members with the community.

To learn more about HSA and its many local chapters and activities, visit the HSA website, <www.herbsociety.org>.

—Karen Robin

NIH Grant Funds Awarded to Bastyr University and Selected Graduates

Bastyr University has received a grant from the National Center of Complementary and Alternative Medicine (NCCAM) at the National Institutes of Health (NIH), as have two outstanding Bastyr graduates. The grants reflects NIH interest in increasing the number of complimentary and alternative medicine (CAM) physicians trained to conduct high-quality, patient-oriented clinical research.

Wendy Weber, N.D., Bastyr University graduate and researcher, received a career development award that will fund her salary for five years and support research development.

This prestigious grant, the first such award granted to a naturopathic physician, is typically given to a medical doctor who is several years removed from medical school. Dr. Weber, however, received her doctorate in naturopathic medicine in June 2001. Between her 1994 graduation from Wesleyan University (psychology/neuroscience and behavior) and her enrollment at Bastyr, Dr. Weber spent three years as a research assistant working on pediatric psychopharmacology research at Massachusetts General Hospital in Boston.

Dr. Weber is a clinical research fellow at the Bastyr Center for Natural Health, where she continues to see patients. Her main research interests are pediatrics and mental health conditions. She is also working toward a master's degree in public health at the University of Washington.

Heather Greenlee, N.D., practices cranio-sacral therapy on her patient, Melea Press of Seattle. Dr. Greenlee received an NIH grant to study ways to prevent breast cancer in women. Photo by Clay Eals, © 2002 Fred Hutchinson Cancer Research Center.

NCCAM Supports CAM Research Training

The NIH grant to Dr. Weber comes in addition to a $1.156 million five-year renewable grant, also from the NCCAM, to train scientists to do research in the field of CAM. Similar grants have been awarded to four conventional medical schools; this is the first to go to a CAM school.

Bastyr serves as the lead institution, in collaboration with the University of Washington, Fred Hutchinson Cancer Research Center, Center for Health Studies at Group Health Cooperative, and Washington State University. The program will accept four postdoctoral fellows during years 1 and 3 of the five-year period. Each postdoctoral fellow will train for three years. Also, six predoctoral students will be accepted each year to study up to three months.

Bastyr is still in the recruitment process, and interested candidates may obtain information from the Bastyr website, <www.bastyr.edu/researchtraininggrant>, or by calling 425/602-3416.

Greenlee and the Hutchinson Center

Heather Greenlee, N.D., a research fellow in Fred Hutchinson's Public Health Sciences Division, received a postdoctoral NIH grant via the Fred Hutchinson Cancer Research Center.

She will research whether there is a safe, effective, alternative to anti-estrogen drugs to prevent breast cancer among women at high risk of the disease.

Greenlee received her doctorate in naturopathy from Bastyr. She continues to see patients at the Bastyr Center for Natural Health, where she is a clinical research fellow. Prior to her enrollment at Bastyr, Greenlee worked as a research assistant at both the Hutchinson Center and the University of Washington, where she is pursuing a master's degree in public health as part of her NIH-funded training.

—Karen Robin

[Bastyr University. First National Institute of Health (NIH) Research Career Development Award for Naturopathic Medicine goes to Bastyr University Graduate [press release]. Kenmore, WA. 2002 April 22.
Bastyr University Receives NIH Funding to Train Scientists in Complementary and Alternative Research [press release]. 2002 March 14.
Fred Hutchinson Cancer Research Center . Seeking a Natural Way to Prevent Breast Cancer [press release]. 2002 Feb. 5.]

Consumers Mix Prescription Meds with Supplements

Researchers from Boston University have expressed concern with unintended interactions that may occur when consumers overlap use of prescription medications with use of herbal or other dietary supplements. Results from the Slone Survey[1] indicate a consistent overlap between conventional and alternative remedies.

Among 2,590 participants (at least 18 years old), 81 percent used at least one medication; 50 percent took at least one prescription drug; and 7 percent took five or more. Herbals and supplements were taken by 14 percent of the population. In addition, 16 percent of prescription drug users admitted to also taking an herbal or supplement.

Reasons for drug use varied widely, with hypertension and headache mentioned most often (9 percent for each). Vitamins and minerals were frequently used for general health (35 percent), as were herbals and supplements (16 percent).

Owing to the relatively high incidence of mixing conventional and alternative remedies, the authors concluded that the overlap raises concern about "unintended interactions." The authors suggested that documenting usage patterns could be used to improve the safety of medication use.

The Slone Survey was a randomized telephone survey of the non-institutionalized American residents in the 48 continental states and the District of Columbia. Data was collected and analyzed from February 1998 through December 1999. The survey questions focused on what medications, by type, were taken during the week preceding the survey date.[2]

1. Kaufman DW, Kelly JP, Rosenberg L, Anderson TE, Mitchell AA. Recent Patterns of Medication Use in the Ambulatory Adult Population of the United States: The Slone Survey. *Journal of the American Medical Association* 2002; 287(3):337-44.
2. Anon. Consumers Mixing Remedies: Herbals and Prescriptions. *Natural Products Industry Insider* 2002 Jan 16.

Agreement to Share Drug Revenues with Samoan Village Sets Benefit-Sharing Precedent

Twenty percent of any commercial revenues from prostratin, an experimental but promising anti-HIV compound, will be returned to the people of Samoa where this plant-derived potential therapy was found, under a precedent-setting agreement.

Prostratin is found in the wood of *Homalanthus nutans* Guill., Euphorbiaceae, a small rainforest tree in Samoa. Paul Alan Cox, Ph.D., Director of the National Tropical Botanical Garden, first collected *H. nutans* in 1984.[1] Before beginning his research, Cox and the Samoan village chiefs agreed that a portion of any future financial benefit would be returned to the village. Cox found that Samoan healers in the village of Falealupo used the bark of the plant to treat hepatitis. He sent their mixtures to the National Cancer Institute (NCI) of the National Institutes of Health (NIH), which isolated prostratin.

AIDS ReSearch Alliance of America (ARA), a non-profit research institution that has helped develop 11 of the current 17 anti-HIV drugs, became interested in prostratin a little over a year ago as the virus continued to development resistance to the current drugs used in Highly Active Anti-Retroviral Therapy (HAART), which is the standard of care for AIDS patients. A study showed that prostratin inhibits HIV replication while activating dormant, or "latent" HIV.[2] Prostratin can stimulate latently infected cells so that the virus may potentially be recognized by the immune system or eradicated by currently available drugs.

After licensing prostratin for HIV therapy from the NCI, Irl Barefield, Executive Director of ARA and Stephen Brown, M.D. ARA's Director of Clinical Research, traveled with Dr. Cox to Samoa where they met with healer's families, village chiefs, and the Prime Minister, Attorney General, and several cabinet members of the Samoan government. Under the terms of the agreement ARA reached with Samoa, 12.5 percent of the profits from prostratin will go to the Government of Samoa, 6.7 percent to Falealupo village, and 0.4 percent to the families of each of the two (now deceased) healers who showed Cox how to use *H. nutans*.[1]

News of the agreement rapidly spread,

Continues on page 55

U.S. Food and Drug Administration Launches New AER Tracking System

The U.S. Food and Drug Administration has launched a new system to report and monitor adverse events reports involving foods, cosmetics and dietary supplements. The new system, under the FDA's Center for Food Safety and Applied Nutrition (CFSAN), is called CFSAN Adverse Events Reporting System (CAERS).

Under the new system, CFSAN will write a letter of notification to the company listed on the product label when the CAERS system receives an adverse event report of illness or injury allegedly associated with the use of a company's product.

The CAERS system will enable FDA to identify potential public health issues associated with a particular product already in the marketplace. FDA will use the information gathered from the system to assist in the formulation and dissemination of CFSAN's post-marketing policies and procedures.

FDA encourages companies to share information with the agency that is relevant and useful concerning adverse events that companies may be aware of involving their product.

The CAERS system replaces the Special Nutritionals/Adverse Event Monitoring System (SN/AEMS) created in 1998. The SN/AEMS website, which included adverse event reports on dietary supplements, has been removed from the FDA website. FDA is currently evaluating how best to incorporate the adverse event data received from the CAERS system into a website for public use.

The CAERS system will be pilot tested this year and is expected to be operational by May 2003. It may not be on the FDA website until 2004. In the meantime, CFSAN's internal adverse event collection and evaluation systems will continue to operate

[American Herbal Products Association. FDA Announces New Adverse Events Reporting System for Dietary Supplements, Food and Cosmetics [press release] 2002 August 29]

Pawpaw Tree Extract Effective against Head Lice

A new shampoo made with compounds from the twigs of pawpaw trees (*Asimina triloba* (L.) Dunal, Annonaceae) has been shown to kill head lice. The product, called PawPaw Lice Remover Shampoo (Nature's Sunshine Products Inc., Spanish Fork, Utah), was introduced after laboratory and clinical studies showed that it was effective.[1]

Of the three types of lice that infest humans, head lice (*Pediculus capitis* deGeer, Pediculidae) are the most prevalent form. The U.S. Centers for Disease control reports that 6 to 12 million people worldwide are infested each year.[2] Head lice are transmitted by person-to-person contact and by sharing articles such as combs, clothing, and pillows. Previous control methods include applying such pesticides as lindane, pyrethrins, permethrin, or malathion, and are resulting in increasingly resistant lice.

Numerous references to other species, also in the family Annonaceae, and including sugar apple (*Annona squamosa* L.) and cherimoya (*Annona cherimola* Mill.), to remove lice are found in folklore.[3] The pawpaw tree produces the largest edible fruit of any native North American tree; some reach more than one pound. Native to eastern North America, pawpaw trees grow wild in the hardwood forests of 26 states in the eastern United States, and they range from northern Florida to southern Canada, and as far west as eastern Nebraska.

Jerry McLaughlin, Ph.D., professor emeritus of pharmacognosy at Purdue University and, currently, vice president for research and development at Nature's Sunshine, has studied the bioactive compounds found in the pawpaw tree since 1976 and has identified a number of very potent compounds, called annonaceous acetogenins, capable of controlling insects and pests.

Pawpaw *Asimina triloba* fruit and seeds Photo ©2002 Nature's Sunshine.

"The pawpaw extract used in this shampoo has more than 50 annonaceous acetogenin compounds," he says. "It's a complicated mixture that this species has evolved to protect itself. The compounds inhibit the mitochondrial production of adenosine triphosphate (ATP), which deprives the pests of energy. Since pesticide resistance requires ATP, resistant pests are especially susceptible."

The formula also includes tea tree oil (*Melaleuca alternifolia* (Maiden & Betche) Cheel, Myrtaceae) and thymol from thyme (*Thumus vulgaris* L., Lamiaceae), which also deplete ATP levels.

"It's been a bit of a struggle to pursue this research in product development because there were no commercial sources of the pawpaw biomass, and to maximize bioavailability, twigs can be collected from the tree only during the month of May," McLaughlin says. "During that time of year, the plants pump up production to protect themselves against pests." He predicts that collection of pawpaw twigs will soon become a new pursuit for wildcrafters and that pawpaw tree plantations will someday produce a commercial crop.

—Karen Robin

1. McCage CM, Ward SM, Paling CA, Fisher, DA, Flynn, McLaughlin JL. Development of a paw paw herbal shampoo for the removal of head lice. *Phytomedicine* 2002. In press.
2. U.S. Centers for Disease Control, Division of Parasitic Diseases. Head Lice Infestation (Pediculosis) Fact Sheet. Accessed online 2002 August <http://www.cdc.gov/ncidod/dpd/parasites/headlice/factsht_head_lice.htm>.
3. Morton JF. *Fruits of warm climates.* Winterville (NC): Creative Resource Systems, Inc.; 1987. p. 65-90.

Sloan-Kettering to Study Kampo Botanical Formula to Treat Liver Cancer

A traditional Japanese formulation comprised of seven Chinese herbs will be studied by Memorial Sloan-Kettering Cancer Center, of New York, to determine its effect against liver cancer. The herbal formulation being tested is called Sho-saiko-to or LiverKampo™ (Honso Pharmaceutical Co., Ltd., Nagoya Japan).

Liver cancer, or hepatocellular carcinoma (HCC), has a poor prognosis, especially when surgical resection is contraindicated. The best treatment for HCC is to remove the tumor surgically. If this option is not possible, some patients may be eligible for ablative therapy, a type of surgery that shrinks the tumor, but does not remove it entirely. One type of ablative therapy, embolization, reduces blood flow in the hepatic artery, the vessel supplying blood to the liver.

Kampo combines multiple raw herbs, according to specific ancient formulas, and then performs an extraction on the entire mixture.

According to the study design on the Sloan-Kettering website <www.mskcc.org>, Sho-saiko-to has been used for many years to treat chronic liver disease. Although there are some reasons to believe that it may be beneficial, Sho-saiko-to has never been evaluated in patients with HCC. Therefore, its risks and benefits are unknown. This study will be assessing the value of Sho-saiko-to in patients who will be undergoing hepatic artery embolization for the treatment of HCC, but who will not be receiving chemotherapy.

Sho-saiko-to is comprised of root of bupleurum (*Bupleurum faclatum* L., Apiaceae), root of pinellia (*Pinellia ternata* (Thunb.) Makino ex Breit., Araceae), rhizhome of ginger (*Zingiberis officinale* Roscoe, Zingiberaceae), root of Chinese skullcap (*Scutellaria baicalensis* Georgi, Lamiaceae), fruits of jujube (*Ziziphus jujuba* Mill., Rhamnaceae), Asian ginseng (*Panax ginseng* C.A. Mey., Araliaceae), root of licorice (*Glycyrrhiza glabra* L. var. *glandulifera* (Waldst. & Kit.) Regel & Herder, Fabaceae).

Sho-Saiko-to's *in vitro*, *in vivo*, and clinical activity seems primarily to inhibit tumor proliferation rather than to kill tumor cells. The Honso USA website <www.honso.com> includes a link to PubMed search results of more than 110 studies and review articles on Sho-saiko-to published from 1995 to 2002 (most of which are conducted on the formula manufactured by another Japanese Kampo manufacturer, Tsumura & Co.).

This clinical trial, under an Investigational New Drug Application (IND) approved by the U.S. Food and Drug Administration, uses a one-stage historical comparison design. Patients scheduled for ablative therapy will be assessed for eligibility and administered 7.5 grams of granular extract per day of Sho-Saiko-to. The outcome used to power the trial is survival at 15 months, the median survival of a historical cohort.

For secondary analyses purposes, liver function, alpha-fetoprotein and intervention-free survival will be compared between the treated cohort and historical data. The patients, approximately 80 in number, will be treated over a two-year period; their progress followed for another year.

"We are very pleased to have had our product selected for study," said Dan Wen, M.D., president of Honso USA, Inc., the American subsidiary of Honso Pharmaceuticals Co., Ltd. based in Tempe, AZ. "And it's an added honor to be able to go directly into a Phase II study due to the overwhelming body of evidence that already exists on the successful use of Sho-saiko-to in the past."

Kampo, Japanese herbal medicine, is part of the East Asian Chinese medicine tradition. Kampo is fundamentally a clinical system based on the classical medical literature dating back to the Han Dynasty in ancient China. In Japan today, 75 percent of physicians use some traditional Kampo formulas, which are available in almost all pharmacies by prescription, or under the advice of specially trained pharmacists. Kampo research in Japan is rigorous by Western standards, in the mold of conventional pharmaceutical research.

Kampo is different from Western herbal medicine, which uses individual herbs or their standardized extraction. Instead, Kampo combines multiple raw herbs, according to specific ancient formulas, and then performs an extraction on the entire mixture. The combination of specific herbs and this extraction process creates a remedy considered by its practitioners to be more effective than the benefit from each herb extracted individually. To emphasize this, Honso product labels state the raw herb amounts before extraction.

—Karen Robin

[Honso USA, Inc. Clinical Phase II Study on Promising Japanese Botanical Formula 'Sho-Saiko-to' For Treating Liver Cancer to Begin in New York (press release). 2002 February 25.]

Heating Garlic Can Reduce Some of Its Biological Activity

Reviewed: Song K, Milner JA. The influence of heating on the anticancer properties of garlic. *American Society for Nutritional Sciences.* 2001 [Supplement]:1054S-1057S.

The potential medicinal value of garlic (*Allium sativum* L., Alliaceae or Liliaceae) has been recognized for thousands of years. The authors cite studies that have shown that garlic has a variety of pharmacologic properties, including hypolipidemic (blood lipid-lowering), hypoglycemic (blood glucose-lowering), antibacterial, antifungal, antioxidant, and anticancer effects.

Support for the anticancer effect of garlic has come from epidemiologic, animal, and laboratory studies. Preclinical research has shown that garlic can protect a number of body tissues against different kinds of carcinogens and can interfere with cancer development at both the initiation and promotion stages. This article reviews research about the effects of heating garlic on its anticancer potential. "Although the minimum daily intake required to reduce cancer risk remains to be determined, garlic has been categorized as a dietary anticarcinogen," the authors write.

Laboratory research suggests that the anticancer substances in garlic include both lipid-soluble and water-soluble sulfur compounds. Garlic is distinguished from many other vegetables because of its high sulfur content, and it is thought that the many allyl sulfur compounds in garlic, including S-allylcysteine (SAC), a water-soluble sulfur-containing amino acid, probably explain many of its medicinal properties.

According to the authors' own research, microwave heating for as little as 30 seconds blocked 90 percent of the activity of alliinase, the enzyme that is activated when garlic is crushed or cut. Alliinase rapidly converts alliin to allicin. Allicin is responsible for garlic's odor, and is considered one of the most important biologically active compounds found in crushed garlic. Microwave heating of garlic for 60 seconds destroyed all alliinase activity. When alliinase is inactivated by heat, alliicin and its derivities cannot be formed. The authors cite studies showing that boiling garlic at 100 degrees C for 20 minutes inactivated its cardiovascular benefits, antifungal effects, antioxidant properties, and ability to inhibit cyclooxygenase (an enzyme that plays a role in the development of some types of cancer).

The authors also performed a study to measure the effects of heating garlic (dosage information was not included in the report) upon a rat anticancer assay. Raw garlic was effective in reducing formation of DNA adducts by 64 percent, and garlic that had been microwaved for 30 seconds provided a similar degree of protection. However, microwaving garlic for 60 seconds destroyed all of its anticancer benefits, whether the garlic had been crushed before heating or not. Letting crushed garlic sit at room temperature for 10 minutes before microwave heating preserved 70 percent of its anticarcinogenic effects, compared with the effects of raw garlic. Cutting the top off of whole, intact garlic and letting it sit for 10 minutes before oven heating also preserved some of its anticancer effects, whereas oven heating for 45 minutes without cutting the top of the garlic destroyed all of its anticarcinogenic potential.

Thus, this research suggests that many of the medicinal effects of garlic are reduced or destroyed by heating. Inactivation of alliinase and other heat-sensitive materials in garlic is probably the mechanism by which heating has this negative effect. "Although garlic is known for its many pharmaceutical effects, these abilities can be depressed by preparation or processing methods," the authors conclude.

—Christina Chase, M.S., R.D.

Pycnogenol® Pine Bark Extract Shows Promise in Diabetic Retinopathy

Reviewed: Spadea L, Balestrazzi E. Treatment of vascular retinopathies with Pycnogenol. *Phytotherapy Research* 2001; 15: 219–23.

This study evaluates whether Pycnogenol® affects the progression of vascular retinal disorders (conditions affecting blood vessels in the retina of the eye), including diabetic retinopathy (disease of the retina caused by diabetes). Pycnogenol (Horphag Research, France) is a patented water extract from the bark of French maritime pine (*Pinus pinaster* Aiton, Pinaceae, syn. *P. maritima* Lam.). The primary active ingredients are flavonoid-type compounds such as catechin, epicatechin, taxifolin, procyanidins, and proanthocyanidins.

Previous research has found that free radicals play an important role in the development of various eye diseases, including retinopathies. Evidence also suggests that antioxidants can be effective at both preventing and treating diseases of the blood vessels in the eye, such as diabetic retinopathy. Previous studies cited by the authors found that antioxidants can inhibit the processes of neovascularization (formation of new blood vessels) and chronic edema (fluid retention) in the retina. Both of these processes, if left unchecked, can cause a loss of vision.

This trial comprised two phases. In the first phase, which was double-blinded, 20 patients were randomly assigned to receive either placebo or Pycnogenol (50 mg, three times daily) for two months. In the second phase, which was open-label, 20 additional patients received Pycnogenol at the same dose schedule and duration. A total of 30 patients took Pycnogenol and 10 took the placebo. All the patients had vascular diseases of the retina due to diabetes, atherosclerosis, hypertension, or thrombosis (blood clot) in the central retinal vein. The majority of the patients had either diabetic or hypertensive retinopathy. The average ages of patients taking placebo and Pycnogenol were 53.1 and 59.7 years, respectively.

The efficacy and safety results of the two phases were analyzed separately and pooled where appropriate. The effects of treatment with Pycnogenol or placebo were assessed using five different parameters: visual acuity, ophthalmoscopy, visual field, fluoroangiography, and pattern electroretinogram. The visual acuity test showed that, on average, placebo-group patients experienced some loss of visual acuity during the two-month study. This indicated that retinopathy can cause rapid deterioration of vision and, therefore, needs prompt treatment. In contrast, Pycnogenol-group patients experienced either a slowing of the deterioration of visual acuity or a small improvement in visual acuity. The difference between the groups was statistically significant ($p < 0.05$ for the right eye and $p < 0.01$ for the left eye).

Ophthalmoscopy, performed to examine the ocular fundus (deepest part of the inside of the eye), showed that Pycnogenol-treated patients had significant improvements from baseline to end of treatment. Placebo-treated patients had no improvement. Field of vision testing showed no changes in either group and no differences between the two groups.

Fluoroangiography showed that patients given Pycnogenol had a significant improvement in the blood-retina barrier, with reduction of vascular permeability (i.e., less leakage from the blood vessels). Placebo patients had no changes during the study according to fluoroangiography.

The electroretinogram (a record of the retinal action currents produced by light stimulus) also showed significant improvements in the Pycnogenol group but no changes in the placebo group. "The results obtained from this objective functional test clearly demonstrate the efficacy of Pycnogenol," the authors say.

No side effects were reported in either group, and Pycnogenol was well-tolerated. The authors conclude that Pycnogenol led to clinical improvement of retinopathy in this study. They discuss the ways this extract appears to have its effects. "The retina is very sensitive to oxygenated free radicals," they note, and therefore the ability of Pycnogenol to scavenge free radicals may explain its beneficial effects. As with many other studies on herbal medicines, the small size of this clinical trial casts its statistical significance in doubt.

French Maritime pine *Pinus pinaster* syn. *P. maritima*
Photo © 2002 Horphag Research Ltd.

In addition, Pycnogenol may have other actions that contribute to its treatment effect. The authors cite a previous study with rats that showed Pycnogenol reduced leakage from the capillaries, strengthening their resistance, other studies that found Pycnogenol decreased capillary permeability or subcutaneous edema in venous disorders, as well as studies that have suggested that diabetic retinopathy may involve abnormalities in localized production of nitric oxide (NO) or reactivity to nitric oxide (a vasodilator). Pycnogenol, like other products that contain antioxidants derived from plants, affects NO activity and, therefore, may influence diabetic retinopathy via this mechanism.

— Christina Chase, M.S., R.D

Press Releases Freely Interpret Failed Study and Claims that St. John's Wort Doesn't Work

by Jerry Cott, Ph.D.

The recent report in the *Journal of the American Medical Association* (*JAMA*) on the National Institutes of Health (NIH)-sponsored study of St. John's wort (*Hypericum perforatum* L., Clusiaceae) in major depression[1] was a disappointment in several respects. The study was a basic three-arm design: St. John's wort (LI-160, Lichtwer Pharma, Berlin; 900–1500 mg/day), sertraline (Zoloft®, Pfizer; 50–100 mg/day), or placebo in 340 patients divided into three equal groups. After eight weeks of treatment, neither treatment had significantly different effects from the placebo group. Judging by the press releases from *JAMA*, Duke University Medical Center (the central research base for this multi-center study that included 12 medical centers), and NIH, the study was a success and proved to the waiting world that St. John's wort (SJW) was ineffective in treating major depression (a category of depression that can be mild, moderate, or severe), despite many previous studies showing that it is effective.[2,3]

The real disappointment was that, not only did SJW fail to relieve symptoms of depression, there was no meaningful discussion of the failure of the FDA-approved antidepressant, sertraline, to work in the same trial. There was also little discussion of the major effect the failure of sertraline (a selective serotonin reuptake inhibitor, or SSRI) had on the interpretation of the study. Not only was the study a disappointment in several respects, but the surrounding publicity has been quite misleading. This is reflected in recent letters to the editor of *JAMA*.[4,5]

As one who was very much involved with initiation of this trial and drafting the first protocol, I believe there has been a disservice to the medical/scientific community as well as to the taxpayers who paid more than $6 million for these data. Since both SJW and sertraline failed to show an effect on either primary outcome measure, the only logical conclusion is that the study was not valid. This conclusion was predetermined by the Research Design section of the NIH protocol that states: "... having an SSRI arm of sertraline will allow an evaluation of the validity of the trial ... ."[1] Elsewhere the protocol design stated, "With only two arms, if the findings cannot discriminate between placebo and hypericum, the results are uncertain regarding failure of the trial or failure of the treatment." From a statistical viewpoint, only the primary outcome measures determine success or failure of a therapeutic trial. Since the study was not valid, from a scientific standpoint, the efficacy of SJW cannot be determined. As pointed out by Steven Bratman, M.D., in the American Botanical Council's press release on this study, resorting to analyses of secondary measures does not resurrect the trial.[6] If secondary outcome measures were valid predictors of efficacy, the Vanderbilt University study published last year in *JAMA* (funded by Pfizer) would have to be interpreted as positive for SJW, since the percentage of patients who recovered was significantly greater in the SJW group than in the control group (14.3 percent vs. 4.9 percent; $p<0.02$).[7] This positive outcome was somehow overlooked in the *JAMA* editorial of the NIH study.[8]

Given that the NIH study was not successful in determining the efficacy of either treatment, is there anything of value that can be gleaned from this considerable research effort? Perhaps this trial could serve as a model for the inherent difficulties in carrying out antidepressant trials where the average failure rate on investigational antidepressant drugs is 50 percent.[9] The authors of this study acknowledged that 35 percent of trials testing "known antidepressants" end in failure.[1]

Of primary concern is the rationale for inclusion of severely depressed patients in this study. The criterion for assessing the severity of depression was initially proposed at a level of 15 or greater on the 17-item Hamilton Depression Rating Scale (HAM-D) scale (mild to moderate depression). This was later raised to the level of 20 or greater (moderate to severe). There appears to be a belief that more severely depressed patients will be less likely to respond to a placebo and thus increase the likelihood of showing a drug/placebo difference.[10] Actual data, however, do not support this belief.[11] The duration of the current episode was also rather long (more than one-third were suffering from depression for a period greater than two years).

A compelling case can be made that chronically depressed patients are less responsive to any treatment, including with known active pharmaceutical drugs, not just placebo. Investigational antidepressant trials conducted by pharmaceutical firms routinely use 17 on the HAM-D as an entry level for trials and avoid the use of chronically depressed patients. The commonality of these entry criteria for other published depression studies was confirmed by the article accompanying the SJW trial in *JAMA* discussing the placebo response, finding a mean HAM-D entry criteria score of 16.7.[11]

The question of the efficacy of SJW in major depression has by no means been settled by the two American clinical trials conducted to date. Rather, they have made it even more clear that the trial that needs to be conducted should follow the design of the one originally proposed (i.e., based on the responses from subjects experiencing mild to moderate major depression).

A recent SJW placebo-controlled trial was published in the *American Journal of Psychiatry*.[2] This trial was performed in France and found a significant antidepres-

sant effect in favor of SJW over placebo. The patient entry criteria was mild to moderate (major) depression with HAM-D scores from 18 to 25. This trial differed from the two American studies in that it was performed at 26 different centers in France, all patients were self-referred (i.e., they were not recruited by newspapers, TV and radio as they are in this country), and there was a severity range on the HAM-D of at least 18 but not more than 25. Unfortunately, the duration of the current episode was not provided.

Jerry Cott, Ph.D., is the former Chief of the Psychopharmacology Research Program at the NIMH and has also been a reviewer of clinical and preclinical studies of antidepressant drugs at the FDA. The study under discussion was funded solely by the NIMH.

References

1. Hypericum Depression Trial Study Group. Effect of *Hypericum perforatum* (St. John's wort) in major depressive disorder: a randomized controlled trial. *JAMA* 2002;287:1807-14.
2. Lecrubier Y, Clerc G, Didi R, Kieser M. Efficacy of St. John's wort extract WS 5570 in major depression: A double-blind, placebo-controlled trial. *Am J Psychiatry* 2002;159(8):1361-6.
3. Whiskey E, Werneke U, Taylor D. A systematic review and meta-analysis of *Hypericum perforatum* in depression: a comprehensive clinical review. *Int Clin Psychopharmacol.* 2001 Sep;16(5):239-52.
4. Cott J, Wisner K. St. John's wort and depressive disorder (letter). *JAMA* 2002;288(4):448.
5. Cott J. NIH St. John's wort study fails to satisfy. *The Integrative Medicine Consult* 2002 July;4(7):73,77,83.
6. American Botanical Council. St. John's Wort study misinterpreted says herbal science group [press release]. 2002 Apr. 9.
7. Shelton RC, Keller MB, Gelenberg AJ, Dunner DL, Hirschfeld R, Thase ME, et al. Effectiveness of St John's wort in major depression: a randomized controlled trial. *JAMA* 2001;285(15):1978-86.
8. Kupfer DJ, Frank E. Placebo in clinical trials for depression: complexity and necessity. *JAMA* 2002;287(14):1853-4.
9. Robinson DS, Rickels K. Concerns about clinical drug trials. *J Clin Psychopharmacol* 2000;20(6):593-6.
10. Schatzberg AF, Kraemer HC. Use of placebo control groups in evaluating efficacy of treatment of unipolar major depression. *Biol Psychiatry* 2000;47(8):736-44.
11. Walsh BT, Seidman SN, Sysko R, Gould M. Placebo response in studies of major depression: variable, substantial, and growing. *JAMA* 2002;287(14):1840-7.

Small Trial Shows Hawthorn Leaf and Flower Extract Is Effective in Early-Stage Congestive Heart Failure

Reviewed: Zapfe G. Clinical efficacy off Crataegus extract WS 1442 in congestive heart failure NYHA class II. *Phytomedicine* 2001; 8:262–6.

In congestive heart failure (CHF), the heart has a reduced ability to pump blood effectively, often due to a previous myocardial infarction (heart attack). This usually causes symptoms such as shortness of breath, weakness, and fluid retention in the legs and feet. "Even mild forms of CHF should be treated adequately to postpone or to prevent progression of the disease," the author writes.

Previous research showed that a hawthorn extract known as WS 1442* (Schwabe Pharmaceuticals, Karlsruhe, Germany) was effective and safe for treating CHF. Clinical studies found that WS 1442 improved exercise tolerance and reduced symptoms of CHF. WS 1442 is made from a dry extract of hawthorn (*Crataegus* spp., Rosaceae) leaves, twigs and flowers.

This randomized, double-blind, placebo-controlled clinical trial was performed to evaluate the efficacy and safety of WS 1442. The study included 40 male and female outpatients, aged 40 to 80 years, with CHF. The severity of their CHF was categorized as New York Heart Association (NYHA) class II, a mild chronic form of CHF. The average age of patients was 58.2 years in the treatment group and 66.5 years in the placebo group. Approximately three-quarters of the patients in both groups were women.

Patients were randomly assigned to receive either placebo or WS 1442 (240 mg per day, divided into 3 doses of 80 mg each) for 12 weeks. WS 1442 was standardized to contain 18.75 percent oligomeric procyanidins. Certain drugs were discontinued, if possible, during the study. These included diuretics, calcium antagonists, ACE inhibitors, cardiac glycosides, and other hawthorn-containing preparations.

At the beginning (baseline) and end of the study, patients underwent exercise tolerance testing on a stationary bicycle. The main outcome variable was exercise tolerance, measured in watts (W) multiplied by minutes (min). The secondary outcome variable was the double product, also known as the pressure-rate product. This is calculated by multiplying heart rate by systolic blood pressure by 10^{-2}. The double product was determined at rest and again after exercising for 2 minutes at a workload of 50 W; the difference between these two values was calculated and used as the difference of the double product.

The results showed that from the start to the end of the 12-week study, average exercise tolerance improved in the treatment group (from 616.3 to 682.5 W x min), but declined in the placebo group (from 623.8 to 527.6 W x min). The difference between groups was of borderline significance ($p < 0.06$) despite average age difference. All 20 patients in the WS 1442 group and 19 of 20 in the placebo group completed the study; one placebo-group patient dropped out due to an allergic skin reaction.

From baseline to end of study, the difference of the double product declined by 26.8 percent in the WS 1442 group but remained unchanged in the placebo group. The change in the WS 1442 group was not significant ($p < 0.11$), yet the author concludes, "this result indicates a positive impact of WS 1442 on exercise tolerance." This reduction in the difference of the double product found in the WS 1442 group may indicate that the heart was using oxygen more efficiently to perform an equivalent amount of work. WS 1442 was shown to be safe and well-tolerated.

The cornerstone of management for CHF is still conventional drug treatment with diuretics, ACE inhibitors, digitalis glycosides, and beta-blockers, based on large-scale trials focusing on such endpoints as mortality. With more research on hawthorn leaf and flower extract, it is possible that this phytomedicine may become more widely adopted in cardiology for CHF Stage II. Hawthorn leaf and flower extract was approved for this indication by the German Commission E in 1994.

—Christina Chase, M.S., R.D.

* WS 1442 is marketed in Germany as Crataegutt® by W. Schwabe and is imported and marketed in the United States as HeartCare® by Nature's Way.

Clinical Update

by Donald J. Brown, N.D.

Using Raspberry Leaf During Pregnancy: A Look at Safety and Efficacy in Labor

Reviewed: Simpson M, Parsons M, Greenwood J, Wade K. Raspberry leaf in pregnancy: its safety and efficacy in labor. *Journal of Midwifery & Women's Health* 2001;46:51-9.

Summary: In a double-blind, randomized, placebo-controlled clinical trial, the effect of raspberry leaf extract in tablets was studied on labor and birth outcomes. The trial included 192 low-risk nulliparous women (mean age of 28.5 years) who were randomized to receive either 400 mg of raspberry leaf (*Rubus idaeus* L., ssp. *idaeus*, Rosaceae) extract (3:1, equivalent to 1,200 mg of dried leaf) or placebo two times per day with food. Patients took raspberry leaf or placebo from 32 weeks gestation until commencement of labor. Commencement of the tablets at 32 weeks gestation was determined according to the most accurate estimate of the woman's last menstrual period and/or earliest ultrasound result. The effects of raspberry leaf consumption were examined by comparing the raspberry leaf and placebo groups for differences in:

1) length of gestation;
2) incidence of induction of labor by syntocinon (an oxytocic drug that stimulates uterine contractions) infusion and artificial rupture of membranes;
3) incidence of medical augmentation of slow labor with syntocinon;
4) incidence of artificial rupture of membranes;
5) use of patient-requested local anesthetic drug and/or epidural block;
6) length of stages of labor; and
7) mode of birth.

The safety of raspberry leaf consumption on pregnancy was measured by analyzing seven different variables, including maternal blood loss, maternal diastolic blood pressure, presence of meconium (the dark green fecal material that accumulates in the fetal intestines and is discharged at the time of birth) stained fluid, newborn APGAR scores (a system of evaluating a newborn's physical condition by assigning a value [0, 1, or 2] to each of five criteria: heart rate, respiratory effort, muscle tone, response to stimuli, and skin color) at 5 minutes, newborn birth weight, newborn admission to neonatal intensive care facilities after birth, and occurrence of side effects reported.

Raspberry leaf was found to have no effect on any stage of labor. After exclusion of mothers who experienced an elective caesarean, it was found that slightly more women in the raspberry leaf group had normal vaginal births (62.4 percent vs. 50.6 percent) and more women in the placebo group had forceps or vacuum-assisted births than would be expected by chance, although not statistically significant ($p = 0.19$). No significant relationship was observed between raspberry consumption and birth outcome. Occurrence of adverse events was distributed equally across the two groups with most adverse events being pregnancy related such as nausea, vomiting, diarrhea and constipation. Raspberry leaf appeared to have no negative effects on either mother or child.

Comments/Opinions: Raspberry leaf — especially in tea form — has long been promoted in traditional herbalism and midwifery as an herbal tonic during pregnancy.[1] Traditionally used throughout pregnancy to treat morning sickness and reduce risk of miscarriage, its primary use has been to strengthen and tone the uterus prior to birth.[2] Anecdotal reports have suggested that uterine contractions during labor may be more coordinated during labor after ingestion of raspberry leaf during the last three months of pregnancy.[3,4]

Attempts to scientifically study raspberry leaf have led to little clarity as to the potential for the herb during pregnancy and some safety concerns. One study found that raspberry leaf extract had different effects on pregnant or non-pregnant rat and human uteri.[5] While the extract had no effect on non-pregnant uterine strips from rats or humans *in vitro*, it inhibited contractions in strips from pregnant rats. However, the extract initiated contractions in strips from pregnant humans at 10 to 16 weeks of pregnancy — with contractions, in most cases, becoming less frequent. An earlier study found that intravenous injection of raspberry leaf extract had a relaxant effect on the uterine muscles of cats.[6] These mixed results have led to some texts suggesting that raspberry leaf be avoided during pregnancy and used only under medical supervision during labor.[7] Since the above research has been primarily *in vitro,* the relevance to humans is unclear. Prior to this trial, published studies on raspberry leaf for pregnancy and labor have been scarce. One study, published in 1941, found that uterine contractions diminished in frequency and strength in women given 20–40 g of raspberry leaf extract in the first few days following birth.[8] A retrospective study, completed by the authors of this new trial in 1998, examined the safety of raspberry leaf tea in women and their babies when consumed during pregnancy.[9] The researchers interviewed 109 postnatal women (day 1–4). Fifty-eight women had consumed raspberry leaf in some form (tea, tablet, tincture), at various dosages, and at various times (as early as 8 weeks gestation to as late as 39 weeks gestation). A control group of 51 women who had not used raspberry leaf were used for comparison. Interestingly, the average length of the first stage of labor was shorter for women consuming raspberry leaf, while the second and third stages were similar in both groups. While these results are not statistically significant, there is a trend in favor of an effect, which may be important when considering pregnancy and labor. The percentage of normal births was 77.2 percent in the raspberry leaf group compared to 66.7 percent in the control group. Obviously, the results of this study are difficult to quantify based on the various levels of raspberry leaf used and the different time of gestation women began taking the herb. Outcomes were similar between groups; no adverse effects attributable to raspberry leaf were noted.

While the results of this new Australian clinical trial may ease concerns about the safety of raspberry leaf prior to labor (e.g., facilitating preterm labor or birth), it does raise questions about the degree of efficacy of the herb for improving labor. Although modest, a slight decrease was noted in the second stage of labor. Additionally, women taking raspberry were slightly more likely to have vaginal births and less likely to require artificial rupture of membranes during labor or forceps to assist birth.

Hopefully, future trials will follow up on this potentially beneficial effect examing a larger population of pregnant women, as well as higher doses of the herb.

Practice Implications: Raspberry leaf extract has a long history of use for pregnant women as an herbal tonic to help ease labor. This new trial suggests that this effect may be minor or non-existent, at least when started in the 32nd week. While certainly not a safety study, the trial suggests that use of raspberry leaf extract beginning at 32 weeks gestation may be safe for both mother and child.

References

1. Foster S. *101 Medicinal Herbs.* Loveland (CO): Interweave Press; 1998. p. 166-7.
2. Clifford T. *Cures.* New York (NY): Macmillan Publishing; 1980. p. 52.
3. Hoffmann D. *The Herbal Handbook: A User's Guide to Medical Herbalism.* Rochester (VT): Healing Arts Press; 1998. p. 151.
4. Mabey R. *The New Age Herbalist.* New York (NY): Macmillan Publishing; 1988. p. 105.
5. Bamford DS, Percival RC, Tothill AU. Raspberry leaf tea: a new concept to an old problem. *Br J Pharmacol* 1970;40:161-2.
6. Burn JH, Withell ER. A principle in raspberry leaves which relaxes uterine muscle. *Lancet* 1941;5:1-3.
7. Newall CA, Anderson LA, Phillipson JD. *Herbal Medicines: A Guide for Health-Care Professionals.* London: Pharmaceutical Press; 1996. p. 226.
8. Whitehouse B. Fragarine: an inhibitor of uterine action. *BMJ* 1941;13:370-1.
9. Parsons M, Simpson M, Ponton T. Raspberry leaf and its effect on labour: safety and efficacy. *Aust Coll Midwives J* 1999;12:20-5.

Saw Palmetto Extract Effectively Manages Lower Urinary Tract Symptoms in Men

Reviewed: Gerber G, Kuznetsov D, Johnson B, Burstein JD. Randomized, double-blind, placebo-controlled trial of saw palmetto in men with lower urinary tract symptoms. *Urology* 2001;58(6):960–65.

Summary: In a randomized, double-blind, placebo-controlled clinical trial, the efficacy of a saw palmetto (*Serenoa repens* (W. Bartram) Small, syn. *Chamaerops serrulata* Michx., *Corypha repens* W. Bartram [basionym], *Sabal dealbata* hort. ex L.H. Bailey, *Sabal serrulata* (Michx.) Nutt. ex Schult. & Schult. f., *Serenoa serrulata* (Michx.) G. Nicholson, Arecaceae) berry extract was tested on urinary symptoms, sexual function, and urinary flow in men with lower urinary tract symptoms (LUTS). Following a 1-month placebo run-in period, 85 men, 45 years of age and older with an International Prostate Symptom Score (IPSS)* of 8 or greater, were randomized to receive 160 mg of saw palmetto berry extract (SPBE), standardized to 85–95 percent fatty acids and sterols (Nutraceutical Corp., Ogden, Utah), or placebo two times per day for 6 months. Patients were evaluated using the IPSS, a quality-of-life questionnaire, a sexual function questionnaire, and by measurement of urinary flow rate. Serum prostate-specific antigen (PSA) was also measured. These measures were completed prior to the placebo run-in period, at baseline and at months 2, 4, and 6. The mean ages of the men completing the 6-month trial were 64.6 (± 9.9) years for the SPBE group (n = 41) and 65.3 (± 9.7) years for the placebo group (n = 44).

The mean IPSS symptom score decreased from 16.7 to 12.3 in the saw palmetto group compared with 15.8 to 13.6 in the placebo group ($p = 0.038$). The quality of life score improved to a greater degree in the SPBE group compared to placebo (0.7 versus 0.3), but was not statistically significant. There was no improvement in the sexual function questionnaire in either group. The peak urinary flow rate increased by 1.0 mL/s in the SPBE group compared to 1.4 mL/s in the placebo group ($p = 0.73$) [Note: While the increase was slightly higher in the placebo group, this difference was not significant. Neither group had a notable increase compared to baseline]. There was no significant change in PSA levels in either the SPBE or placebo groups. Only one adverse event was reported — mild gastric distress in one patient in the SPBE group.

Comments/Opinions: This is the second saw palmetto study to be completed by Glenn Gerber, M.D., and colleagues at the University of Chicago Pritzker School of Medicine in Chicago. The first, a 6-month, open-label, nonrandomized study using the same preparation and dose of SPBE, found results similar to the placebo-controlled trial summarized above — an improvement on the mean IPSS (7 points) but no improvement in peak urinary flow.[1] Interestingly, the earlier trial also found no change in mean serum levels of prostate specific antigen (PSA) in those men taking saw palmetto.

Gerber and colleagues have taken a novel approach to their studies of saw palmetto. While the majority of clinical trials published to date have focused primarily on men with urinary tract symptoms secondary to clinically confirmed benign prostatic hyperplasia (BPH), Gerber's studies have focused primarily on men with a diagnosis of LUTS who may or may not have accompanying BPH. This strategy presents a bit of a paradox — while looking at men with LUTS may approximate the larger population choosing to self-medicate with saw palmetto, it creates a more diverse study population, making evaluation of the outcome more difficult. This is particularly the case when peak urinary flow is used as one of the primary outcome measures as many of the men included in his studies had peak urinary flow of 15 mL/s or greater — essentially in the normal range.

During the 1990s, considerable debate began to arise among urologists as to how to categorize those men with urinary tract symptoms and clinically identified BPH (e.g., an enlarged prostate) versus those men with urinary tract symptoms in the

*Note: The International Prostate Symptom Score (IPSS) is based on seven questions regarding urinary tract symptoms associated with benign prostatic hyperplasia. These symptoms include urgency, daytime and nighttime urinary frequency, hesitancy, intermittency, sensation of incomplete voiding, and force of urine stream.

A naturopathic physician, Donald Brown is one of the leading authorities in the U.S. on evidence-based herbal medicine. An associate professor at the Bastyr University of Natural Health Sciences in Seattle, he is the founder and director of Natural Product Research Consultants, Inc. and serves on ABC's Advisory Board as well as the President's Advisory Board of Bastyr University. He has also served as an advisor to the Office of Dietary Supplements at the National Institutes of Health.

Clinical Update

by Donald J. Brown, N.D.

absence of BPH. The consensus was to use the terminology *lower urinary tract symptoms* or LUTS to describe the collection of symptoms listed on the IPSS.[2] While the consensus regarding classification has become largely accepted, the etiology of LUTS or BPH remains cloudy.

It's interesting to note that the class of drug that has most successfully treated LUTS has been the alpha-adrenergic receptor blockers (e.g., Cardura®, Flomax®, and Hytrin®) and not the 5-alpha-reductase inhibitor finasteride (Proscar®). While studies have favorably compared SPBE, either alone or in combination with stinging nettle root (*Urtica dioica* L. ssp. *dioica*, Urticaceae), with finasteride in the treatment of urinary tract symptoms associated with BPH,[3,4] the results of Gerber's trials suggest that the more interesting comparison should be with alpha-adrenergic receptor blockers.

It's important to note that although debate continues about the quality of some clinical trials examining the efficacy of SPBE for BPH, the consensus of at least two meta-analyses indicate that the herbal extract does improve both peak urinary flow as well as urinary tract symptoms in men with BPH.[5,6] It is unclear from this study how many men actually had BPH versus those with LUTS in the absence of BPH.

Hopefully, future clinical trials will focus on the use of SPBE for LUTS over a more extended period and, as mentioned above, add a comparison with the more commonly used alpha-blockers. These trials will hopefully expand the clinical understanding of where SPBE may lie in the spectrum of available treatments for LUTS.

Practice Implications: This U.S. clinical trial suggests that a liposterolic extract of saw palmetto berries may be a safe and efficacious treatment option for the management of LUTS in men over 45 years of age. While successful trials with SPBE for BPH have found an improvement in peak urinary flow, this trial failed to find any effect. This may be partly explained by the fact that many of the men entered in this trial had normal flow rates (> 15 mL/s) while other trials have typically studied men with abnormal flow rates (<15 mL/s) typically seen in BPH.

References

1. Gerber GS, Zagaja GP, Bales GT, et al. Saw palmetto (*Serenoa repens*) in men with lower urinary tract symptoms: Effects in urodynamic parameters and voiding symptoms. *Urology* 1998;51:1003–7.
2. Denis LJ. Editorial review of "Comparison of phytotherapy (Permixon®) with finasteride in the treatment of benign prostatic hyperplasia: A randomized international study of 1098 patients." *Prostate* 1996;29:241–2.
3. Carraro JC, Raynaud JP, Koch G, et al. Comparison of phytotherapy (Permixon®) with finasteride in the treatment of benign prostatic hyperplasia. *Prostate* 1996;29:231–40.
4. Sökeland J, Albrecht J. A combination of Sabal and Urtica extracts versus finasteride in BPH (stage I to II acc. to Alken): A comparison of therapeutic efficacy in a one-year study. *Urologe [A]* 1997;36:327–33.
5. Wilt TJ, Ishani A, Stark G, et al. Saw palmetto extracts for treatment of benign prostatic hyperplasia. A systematic review. *JAMA* 1998;280:1604–9.
6. Boyle P, Robertson C, Lower F, Roehrborn C. Meta-analysis of clinical trial of Permixon in the treatment of symptomatic benign prostatic hyperplasia. *Urology* 2000;55:533–9.

Treating Seasonal Allergic Rhinitis with Butterbur Extract

Reviewed: Schapowal A. Randomised controlled trial of butterbur and cetirizine for treating seasonal allergic rhinitis. *BMJ* 2002;321:1–4.

Summary: One hundred thirty male and female patients (aged 18 years or older) with a history of seasonal allergic rhinitis (at least two consecutive years) were screened for a randomized, double blind trial comparing the efficacy of a butterbur extract and cetirizine (a non-sedating antihistamine). One hundred twenty-five patients were randomized to take either one butterbur (*Petasites hybridus* (L.) P. Gaertn. et al., Asteraceae) herb extract tablet (standardized to 8.0 mg of total petasin per tablet, ZE 339, Zeller AG, Switzerland)* four times per day or one 10 mg tablet of cetirizine in the evening. Blinding was achieved by having each patient take five tablets — four containing either placebo or butterbur, and one containing either cetirizine or placebo — depending on the treatment group. The main outcome measure was change of score from baseline of each item on the medical outcome health questionnaire (SF-36). The SF-36 questionnaire is a self-assessment tool with questions grouped hierarchically in eight categories with a total range of 0–100 per item. The questionnaire also includes one category with a five-point score for comparing current severity of the condition with that of the previous year. The secondary outcome measure was the physician's clinical global impression scale (CGI). The hypothesis was that butterbur was roughly equivalent to cetirizine at the end point, defined as within 10 percent of the SF-36 score or by one point in the CGI.

Improvements in both the SF-36 and CGI scores were similar in both groups. Analysis of the main outcome measures rejected the hypothesis of butterbur's being inferior to cetirizine, with none of the scores in the butterbur group more than 10 percent worse than in the cetirizine group. The overall incidence of adverse events was similar for the two treatment groups. However, two-thirds of the adverse events for the cetirizine group were drowsiness and fatigue — symptoms not reported in the butterbur group.

Comments/Opinions: Allergic rhinitis (sometimes called hay fever) can be either seasonal or perennial and is characterized by sneezing, runny nose, nasal congestion, throat itching and irritation, and watery eyes. The allergic response is typically caused by the deposition of an allergen (e.g., pollen) on the nasal membranes. Typical treatment is the symptomatic use of over-the-counter antihistamines (e.g., clorpheniramine, diphenhydramine) or the new generation of prescription antihistamines such as loratadine (Claritin®, Schering Corporation, Kenilworth, NJ) or desloratadine (Clarinex®, Schering Corporation). While usually safe, antihistamines may cause drowsiness (please note that the last two products mentioned above are not associated with drowsiness) and may also interact with alcohol and can sometimes lead to complaints of dryness in the nasal passages and throat. The availability of an over-the-counter nasal spray containing cromolyn sodium (NASALCROM™, Pharmacia, Peapack, NJ) has offered allergic rhinitis sufferers a non-sedating

*Note: The total milligram amount of extract per tablet is not listed in the publication.

alternative that helps stabilize mast cells (the cells that release histamine in the mucous membranes of the nose and sinuses) and can act as a preventive agent. Nasal steroids are another treatment option for allergic rhinitis sufferers.

Research-supported herbal alternatives for the management of allergic rhinitis are scarce. Small clinical trials have suggested that freeze-dried stinging nettle (*Urtica dioica* L. ssp. *dioica*, Urticaceae)[1] and the Japanese Kampo medicine *sho-seiryu-to* — a combination of licorice root (*Glycyrrhiza glabra* L., Fabaceae), cassia bark (*Cinnamomum aromaticum* Nees, Lauraceae), schisandra (*Schisandra sphenanthera* Rehder & E.H. Wilson, Schisandraceae), ephedra or *ma huang* (*Ephedra sinica* Stapf, Ephedraceae), ginger root (*Zingiber officinale* Roscoe, Zingiberaceae), pinellia (*Pinellia ternata* (Thunb.) Makino ex Breit., Araceae), and asiasarum root[2] (*Asiasarum* is an outdated name for certain Asian species of *Asarum*. The two species used interchangeably (as *Xi Xin*) in Traditional Chinese Medicine for colds are *Asarum heterotropoides* F. Schmidt var. *mandshuricum* (Maxim.) Kitag. and *Asarum sieboldii* Miq., Aristolochiaceae.) may hold promise for the treatment of allergic rhinitis. However, there have been no follow-up studies on these products.

Petasites hybridus is an herbaceous plant of the family Asteraceae native to Europe, northern Africa, and southwestern Asia.[3] Although the name butterbur is used as the common name in this study, its standardized common name is purple butterbur and it is also commonly called sweet coltsfoot.[4] A related plant, *P. frigidus* (L.) Fries, is known commonly as Arctic butterbur and less commonly as Arctic sweet coltsfoot or western coltsfoot — and should not be confused with coltsfoot (*Tussilago farfara* L., Asteraceae).

The leaves, rhizome, and roots of butterbur contain a mixture of eremophilan-type sesquiterpenes consisting primarily of petasin and isopetasin.[3] Renowned German phytotherapy experts Rudolf Fritz Weiss, M.D., and Volker Fintelmann, M.D., suggested that petasin has both spasmolytic and analgesic actions.[5] They wrote that this explains the historical use of the plant for whooping cough and bronchial asthma. Interestingly, the German Commission E has separate monographs for butterbur leaf and rhizome. The leaf is given a negative rating due to the assessment that other herbal drugs were more effective in relieving cough, such as thyme (*Thymus vulgaris* L., Lamiaceae) or sundew (*Drosera rotundifolia* L., Droseraceae).[6] Butterbur rhizome, on the other hand, receives a positive rating for the adjunctive treatment of acute spasmodic pain in the urinary tract.[7] I was unable to find any historical references to the herb's use for allergic rhinitis.

The dark cloud hanging over butterbur leaf and rhizome is the presence of toxic pyrrolizidine alkaloids (PAs).[8] These potentially hepatotoxic and carcinogenic constituents have led to the demise of coltsfoot and comfrey root (*Symphytum officinale* L., Boraginaceae) in herbal medicine as well. Drs. Weiss and Fintelmann suggest that this has been the primary explanation for the waning interest in the therapeutic use of butterbur.

The ZE 339 extract used in this trial is from the aerial parts of the herb and not the rhizome of the plant. Perhaps most important, the manufacturers remove PAs during the manufacturing process.[9] While the butterbur product used in this trial is currently unavailable in the U.S., a product made from the rhizome and delivering 7.5 mg of total petasin per capsule is commercially available (Petadolex™, Weber and Weber, USA). Also a CO_2 extract, the Petadolex product is also free of PAs. While this product has been studied for treating migraine,[10,11] it has not been studied for treatment of allergic rhinitis.

Practice Implications: Although this trial lacks a placebo group for comparison, it suggests that butterbur extract may be as effective as the antihistamine cetirizine for the management of symptoms associated with seasonal allergic rhinitis. One advantage of the butterbur extract appears to be the absence of sedating side effects associated with many antihistamines. Placebo-controlled trials are needed as well as more safety information on the long-term use of butterbur extract.** Again, healthcare professionals should use caution to ensure that any butterbur extract recommended is free of PAs.

References

1. Mittman P. Randomized double-blind study of freeze-dried *Urtica dioica* in the treatment of allergic rhinitis. *Planta Med* 1990;56:44–7.
2. Baba S, Takasaka T. Double-blind clinical trial of sho-seiryu-to (TJ19) for perennial nasal allergy. *Clin Otolaryngol* 1995;88:389–405.
3. Wichtl M. Bisset NG, translator. *Herbal Drugs and Phytopharmaceuticals*. Boca Raton (FL): CRC Press; 1994. p. 366–8.
4. McGuffin M, Kartesz JT, Leung AY, Tucker AO, editors. *Herbs of Commerce, 2nd edition*. Silver Spring (MD): American Herbal Products Association; 2000. p. 109.
5. Weiss RF, Fintelmann V. *Herbal Medicine, 2nd edition*. Stuttgart, Germany: Thieme; 2000. p. 200–2.
6. Blumenthal M, Busse WR, Goldberg A, et al, editors. *The Complete Commission E Monographs: Therapeutic Guide to Herbal Medicines*. Integrative Medicine Communications: Boston (MA); 1998. p. 365.
7. Blumenthal M, Busse WR, Goldberg A, et al, editors. *The Complete Commission E Monographs: Therapeutic Guide to Herbal Medicines*. Integrative Medicine Communications: Boston (MA); 1998. p. 183.
8. Gruenwald J, Brendler T, Jaenicke C, editors. *PDR for Herbal Medicines*. Montvale (NJ): Medical Economics; 2000. p. 585–8.
9. Boonen G (Zeller AG). Personal correspondence to Blumenthal M. 2002 April 24.
10. Lipton RB, Gobel H, Wilkes K, Mauskop A. Efficacy of Petasites (an extract from Petasites rhizome) 50 and 75 mg for prophylaxis of migraine: Results of a randomized, double-blind, placebo-controlled study. *Neurology* 2002;58(suppl 3):A472 [Presented at the 44th Annual American Headache Society Meeting, June 22, 2002, Seattle, WA].
11. Grossmann M, Schmidramsl H. An extract of *Petasites hybridus* is effective in the prophylaxis of migraine. *Inter J Clin Pharmacol Ther* 2000;38:430–5.
12. Shuster S. Treating seasonal allergic rhinitis: Well designed experiments should have been used (letter). *BMJ* 2002;324:1277.
13. Treating seasonal allergic rhinitis: Trial does not show that there is no difference between butterbur and cetirizine (letter). *BMJ* 2002;324:1277.
14. Schapowal A. Treating seasonal allergic rhinitis: Author's reply (letter). *BMJ* 2002;324:1277.

** Note: Following the completion of this review, there have been many letters to the editor of *BMJ* criticizing the design of this trial.[12,13] In one response, one of the authors of the trial refers to the completion of a double-blind, placebo-controlled trial of the butterbur extract for allergic rhinitis which has been submitted for publication.[14]

King oyster mushroom (*Pleurotus eryngii*). An edible and medicinal species that demonstrates immunomodulating and hypocholesterolemic activities. Photo courtesy of the author.

Review of Medicinal Mushrooms Advances

Good News from Old Allies

by Solomon P. Wasser, Ph.D., Dr.Sci. (Biol.)

Edible and medicinal mushrooms (macrofungi) not only can convert the huge lignocellulosic biomass* waste into human food, but — most remarkably — can produce notable mycopharmaceuticals, myconutriceuticals and mycocosmeceuticals.

The most significant aspect of mushroom cultivation, if managed properly, is to create zero emission of lignocellulosic waste materials. Mushroom biotechnological products have multibeneficial effects to human welfare (e.g., as food, health tonics and medicine, feed and fertilizers, and to protect and regenerate the environment). Pharmaceutical substances with potent and unique health-enhancing properties were isolated recently from medicinal mushrooms and distributed worldwide.[2] Many of them are pharmaceutical products, while others represent a novel class of dietary supplements or "nutraceuticals." Several antitumor polysaccharides, such as hetero-ß-glucans and their protein complexes (e.g., xyloglucans, and acidic ß-glucan containing uronic acid) as well as dietary fiber, lectins, and terpenoids, have been isolated from medicinal mushrooms. In Japan, China, Russia, and Korea, several different polysaccharide antitumor drugs have been developed from the fruiting bodies, mycelia, and culture media of various medicinal mushrooms, such as shiitake (*Lentinus edodes* (Berk.) Sing., Tricholomataceae), reishi (*Ganoderma lucidum* (Curt.:Fr.) P. Karst., Ganodermataceae), turkey tail (*Trametes versicolor* (L.:Fr.) Lloyd, Polyporaceae), split gill (*Schizophyllum commune* Fr.:Fr., Schizophyllaceae), mulberry yellow polypore (*Phellinus linteus* (Berk. et Curt.) Teng., Hymenochaetaceae), and chaga or cinder conk (*Inonotus obliquus* (Pers.:Fr.) Pilat, Hymenochaetaceae). The potential of medicinal mushrooms is enormous but mostly untapped. It could and should evolve into a successful biotechnological industry for the benefit of humankind.

The study of medicinal mushrooms through the last three decades has proved its many beneficial outcomes and has been followed by the rapid development of manufacturing businesses dealing with commercial cultivation of mushrooms. In 1999, world production of mushrooms amounted to US$18 billion, roughly equal to the value of coffee sales.[3,4]

Medicinal mycology has deep and firm roots in fungi's traditional uses in the medicine of the Far East. For centuries, Chinese and other healthcare practitioners employed mushrooms to treat various diseases. They valued the power of some mushrooms as divine (e.g., a special goddess was associated with the reishi mushroom). Reishi is also considered a symbol of happy augury and good future, good health, longevity, and even life with the immortals. The use of medicinal mushrooms has gone beyond medicine itself: different schools of Taoism employed reishi and other mushrooms as purifiers and promoters of mind and spirit.[5]

Only at the end of the 1960s did Eastern and Western scientists start to investigate the mechanisms of the health effects of mushrooms. The first successful research discovered the antitumor effects of hot water extracts from several mushroom species.[6] The main active components proved to be polysaccharides, specifically ß-D-glucans. Chihara and his co-workers[7] isolated from the fruiting bodies of shiitake a water-soluble antitumor polysaccharide, which was named "lentinan" after the

Above: **Royal sun *Agaricus*** (*Agaricus blazei*) is a culinary-medicinal mushroom, and a new star in the potential treatment of cancer. Photo courtesy of the author.

* Biomass includes the full range of plants and plant-derived materials, such as dedicated energy crops and trees, agricultural food and feed crops, agricultural crop wastes and residues, wood wastes and residues, and municipal wastes. The majority of non-food biomass is composed primarily of the natural polymers cellulose, hemicellulose, and lignin and is referred to as lignocellulosic biomass. Lignocellulose is a complex of lignin and cellulose present in the cell walls of woody plants. Lignin is a complex organic polymer deposited in the cell walls of plants, making them rigid and woody. Lignocellulosic material resource, like solar energy, is sustainable. Lignocellulosic material is a kind of biomass that is estimated to amount to 1.9×10^{11} tons of dry matter on land annually.[1]

generic name of this mushroom. This was a major discovery. Lentinan demonstrated powerful antitumor activity; preventing chemical and viral tumor development in mice and experimental models.[8,9]

Polysaccharides displaying remarkable antitumor activity *in vivo* (i.e., through screening against sarcoma 180 in mice using intraperitoneal or oral methods of administration) have been isolated from various species of mushrooms belonging to the orders Auriculariales, Tremellales, Polyporales, and Gasteromycetales.[2,6,8,10-13]

Since the discovery of lentinan, several antitumor polysaccharide agents have been developed and commercialized, using the submerged cultured mycelial biomass of turkey tail (Krestin, PSK; Japan), and liquid cultured broth product of split gill (Sonifilan, SPG, Schizophyllan; Japan). These antitumor substances are regarded as biological response modifiers that activate immunological responses. This basically means that:

1) they cause no harm and place no additional stress on the body;

Shiitake *Lentinus edodes* ©2002 Paul Stamets

2) they help the body to adapt to various environmental and biological stresses;
3) they have nonspecific action on the body, supporting some or all of the major systems, including nervous, hormonal, and immune systems, as well as regulatory functions.

It is, indeed, fair to describe all major medicinal mushroom preparations, both cellular compounds and secondary metabolites, as having weak antigenicity and no side effects.

A very popular and effective preparation was developed from turkey tail in Japan as early as 1965. A polysaccharide-peptide from this mushroom, under the name Krestin (PSK), was developed from the strain CM-101. It was approved for use against a number of cancers and was covered by the Japanese healthcare plan. PSK exhibits a marked effect against different types of tumors in experimental animals when administered intraperitoneally or orally. PSK contains 75 percent glucan and 25 percent protein. In 1993, Krestin comprised 25 percent of the anticancer drug market in Japan, and sales totaled US$350 million.[10,14] An analogous product under the name Polysaccharide Peptide (PSP) was developed in China from turkey tail strain Cov-1; the development process for this strain lasted nine years, from 1983 to 1992.[15] Mizuno[11] stated that, in general, a period of 10 years and a total US$75 million, or 10 billion yen, are required from the beginning of development of a new drug to the time it is marketed.

Another ß-D-glucan developed and popular in Japan is schizophyllan from split gill. It is especially effective against cervical cancer.[11] A glucan from mulberry yellow polypore was developed recently in Korea, and an analogous polysaccharide biotechnology from this species has been accomplished in Japan.[16]

Reishi, already mentioned as a sacred mushroom in ancient China, has come to occupy a leading place in present-day medicinal mushroom development. The market values of reishi-based natural healthcare products in 1995 were estimated as US$215 million in Taiwan, US$350 million in China, US$600 million in Korea, and US$350 million in Japan.[5] The physiologically active substances of reishi are water-soluble polysaccharides and alcohol-soluble triterpenoids. Today, 119 different triterpenoids are identified in reishi,[12] about 80 of which are biologically active. Reishi dietary supplements (DS) are valued for their immunomodulating, anticancer, antiviral properties. They are used during remission of cancer and by hepatitis B patients. They also have anti-hyperlipidemic, hypotensive, and hypoglycemic actions.[17]

Some 30 years ago, epidemiologists studying the native population in the Piedade region in the suburbs of San Paulo, Brazil, noted that the rate of occurrence of adult diseases was extremely low, and found an association with the *Agaricus* species, which was a part of the regular diet of the inhabitants of this area.[18] This mushroom was identified as *A. blazei* Murr., known by common names royal sun *Agaricus*, *himematsutake*, *kawarihaaratake*, or almond-flavored portobello. Experiments conducted in Japan with mice verified that *A. blazei* significantly activates the immune system.[18] A number of immunity-enhancing, anticancer, and antitumor fractions were isolated from *A. blazei*. This species was shown to be the most effective anticancer mushroom in a study comparing its effects with shiitake, maitake (*Grifola frondosa* (Dicks.:Fr.) S.F. Gray, Polyporaceae), reishi, and other medicinal mushrooms. Fractions identified with immune effects include polysaccharides, (1→6)-(1→3)-β-D-glucans, (1→6)-(1→4)-β-D-glucans, polysaccharide-protein complex (ATOM), RNA-protein complexes, and glucomannan.[13,18-23]

The Japan Cancer Association proved that *A. blazei* is effective against Ehrlich's ascites carcinoma, sigmoid colon cancer, ovarian cancer, breast cancer, lung cancer, and liver cancer, as well as against solid cancers.[18]

Higher Basidiomycetes mushrooms contain a large amount of well-balanced essential amino acids. Dietary fibers are abundant in the tissue of all mushrooms; they absorb bile acids or hazardous materials in the intestine, and thus decrease the chances of carcinogenic and other poisoning. The overall harmonizing effect of

a diet balanced with mushroom, so highly praised by the ancient Chinese, is not a myth, but is continually supported by modern scientific investigations.

Several other health-promoting effects of the mushrooms should not be overlooked. Not only polysaccharides and triterpenoids are known as biologically active; wide ranges of substances from higher Basidiomycetes belonging to different classes of chemical compounds have been described and their medicinal properties evaluated. These substances represented glycolipids (schizonellin), compounds derived from the shikimic acid (strobilurins and oudemansins), aromatic phenols (drosophilin, armillasirin, omphalone), fatty acid derivatives (filiboletic acid, podoscyphic acid), polyacetylenes (agrocybin, xerulin), polyketides (caloporoside, hericenones A-H), nucleosides (clitocine, nebularine), different sesquiterpenes (protoilludanes, marasmanes, hirsutanes, caryophyllanes, etc.), diterpenes (cyathin, striatal), sesterterpenes (aleurodscal), and many other substances of different origin.[2,10,24]

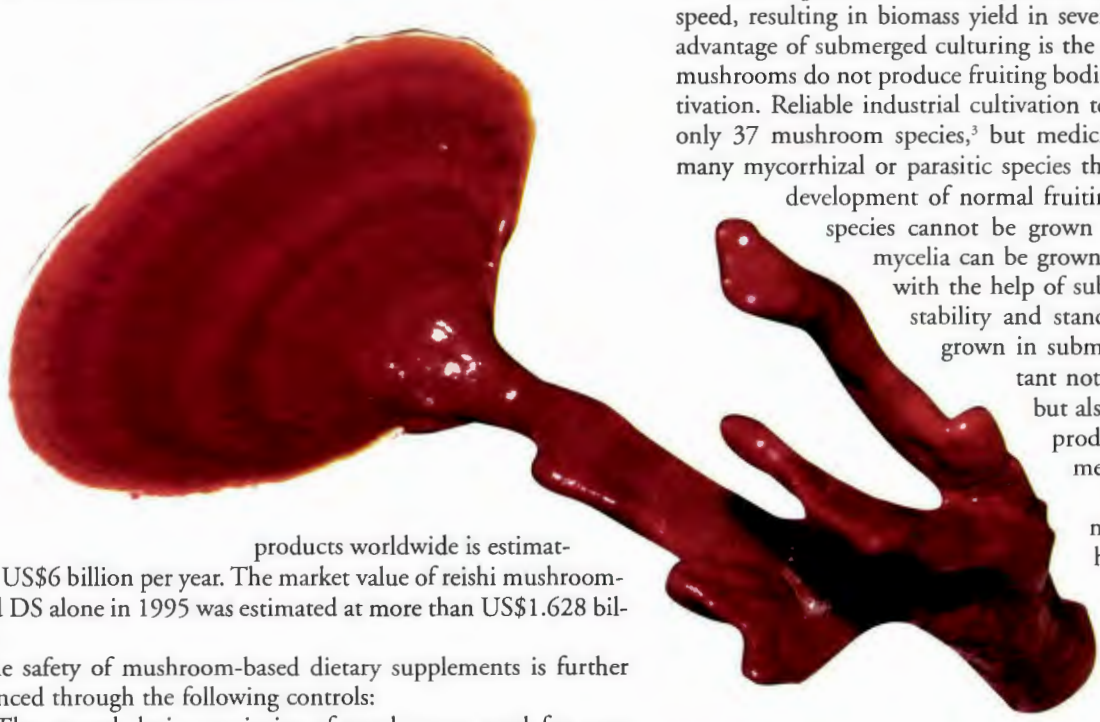
Biologically active substances from higher Basidiomycetes possess antifungal, antibacterial, and antiviral properties; they can be used as insecticidal and nematocidal agents. In medicine they are used to immunomodulate both humoral and cellular immune factors in the body. Polyfunctional acidic glucuronoxylomannan isolated from jelly mushrooms (*Tremella* spp., Tremellaceae), for instance, stimulates vascular endothelial cells, possesses pronounced antiradiating effects, stimulates hematogenesis, demonstrates antidiabetic, anti-inflammatory, hypocholesterolemic, anti-allergic activities, and shows hepatoprotective effects. It can be recommended to improve immunodeficiency, including that induced by AIDS, physical stress or aging, and it prevents senile degeneration of microvessels, maintaining better blood perfusion conditions in vital organs.[4]

Below: **Shiitake** *Lentinus edodes* ©2002 Paul Stamets

Most mushroom-derived preparations and substances find their use not as pharmaceuticals, but as a novel class of dietary supplements or "nutraceuticals." A mushroom nutraceutical is a refined or partially refined extract or dried biomass from either the mycelium or the fruiting body of the mushroom, which is consumed in the form of capsules or tablets as a dietary supplement (not a conventional food) and which has potential therapeutic applications. Regular intake may enhance the immune responses of the human body, thereby increasing resistance to disease, and in some cases, causing regression of a disease state. The market value of mushroom DS

Turkey tail or yun zhi (*Trametes versicolor*). This medicinal species contains antitumor polysaccharide which was used for producing an anti-digestive organ, lung, and breast cancer drug (Krestin) in Japan. Photo courtesy of the author.

Reishi *Ganoderma lucidum* ©2002 Paul Stamets



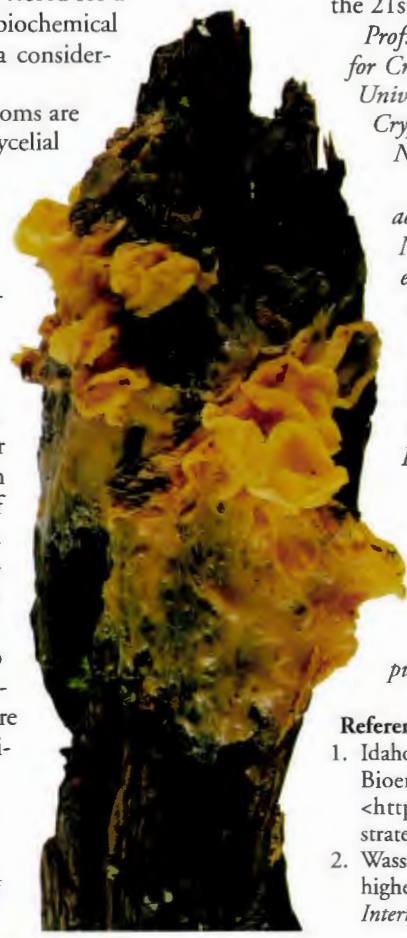
products worldwide is estimated at US$6 billion per year. The market value of reishi mushroom-based DS alone in 1995 was estimated at more than US$1.628 billion.[5]

The safety of mushroom-based dietary supplements is further enhanced through the following controls:

1. The overwhelming majority of mushrooms used for production of DS are cultivated commercially (and not gathered in the wild). This guarantees proper identification, and pure, unadulterated products. In many cases it also means genetic uniformity. This may also benefit conservation of biodiversity.
2. Mushrooms are easily propagated vegetatively, and thus keep to one clone. The mycelium can be stored for a long time, and the genetic and biochemical consistency may be checked after a considerable period of time.
3. Many edible and medicinal mushrooms are capable of growing in the form of mycelial biomass in submerged cultures.[4]

This last aspect, in our experience, offers a promising future for standardized production of safe mushroom-based DS. Submerged culture and semi-solid state fermentation has more consistent and predictable composition than that of fruit bodies. For most substances, this mycelium biomass obtained by submerged cultivation also has higher nutritional value. The culture media in which mycelium grows are made of chemically pure and ecologically clean substances. The cultivation of mushrooms for fruit body production is a long-term process, taking one to several months for the first fruiting bodies to appear, depending on species and substrate. By contrast, the growth of pure mushroom cultures in submerged conditions in a liquid culture media permits acceleration of the growth speed, resulting in biomass yield in several days.[4] The additional advantage of submerged culturing is the fact that most medicinal mushrooms do not produce fruiting bodies under commercial cultivation. Reliable industrial cultivation techniques are known for only 37 mushroom species,[3] but medicinal mushrooms include many mycorrhizal or parasitic species that need several years for development of normal fruiting bodies on trees. Such species cannot be grown commercially, but their mycelia can be grown easily and economically with the help of submerged culturing. High stability and standardization of mycelium grown in submerged cultures is important not only for producing DS, but also might be beneficial for producing mushroom-based medicines.

The use of medicinal mushrooms goes hand in hand with development of their artificial cultivation. The most significant aspect of mushroom cultivation, if managed properly, is to create zero emissions (no waste). Since more than 70 percent of agricultural and forest materials are non-productive and are wasted in processing, this is a very real advantage.[25] Many of these waste materials can be used as substrates to grow mushrooms. This fact gives a basis to the opinion of many researchers in the field (including this author) that sustainable development of mushrooms and their products in the 21st century can become a "non-green revolution."[3]



Yellow brain mushroom (*Tremella mesenterica*). This edible and medicinal species demonstrates antidiabetic, antiinflammatory, hypocholesterolemic, antiallergic activities. Photo courtesy of the author.

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In addition to his scientific studies, Prof. Wasser performs a number of public and social activities. He is a founder and editor-in-chief of three international journals, Algologia *(Ukraine),* International Journal of Medicinal Mushrooms *(USA) and* International Journal on Algae *(USA). He is an author and co-author of 400 scientific publications, including 35 books and 12 patents.*

References:

1. Idaho National Engineering and Environmental Laboratory. INEEL Bioenergy Initiative. 2001 July. Available online: <http://www.inel.gov/energy/bioenergy/web-version-bioenergy-strategic-initiative-dnt-v2.pdf>
2. Wasser SP, Weis AL. Medicinal properties of substances occuring in higher Basidiomycetes mushrooms: Current perspectives [Review]. *International Journal of Medicinal Mushrooms* 1999;1:31-62.

3. Chang ST. Global impact of edible and medicinal mushrooms on human welfare in the 21st century: nongreen revolution. *International Journal of Medicinal Mushrooms* 1999;1:1-8.
4. Wasser SP, Nevo E, Sokolov D, Reshetnikov S, Timor-Tismenetsky M. Dietary supplements from medicinal mushrooms: diversity of types and variety of regulations. *International Journal of Medicinal Mushrooms* 2000;2:1-19.
5. Chang ST, Buswell JA. *Ganoderma lucidum* (Curt.:Fr.) P.Karst. (Aphyllophoromycetideae) – a mushrooming medicinal mushroom. *International Journal of Medicinal Mushrooms* 1999;1:139-48.
6. Ikekawa T, Uehara N, Maeda Y, Nakanishi M, Fukuoka F. Antitumor activity of aqueous extracts of edible mushrooms. *Cancer Res* 1969;29:734-5.
7. Chihara G, Maeda Y, Hamuro J, Sasaki T, Fukuoka F. Inhibition of mouse sarcoma 180 by polysaccharides from *Lentinus edodes* (Berk.) Sing. *Nature* 1969;222:687-8.
8. Zakany J, Chihara G, Fachet J. Effect of Lentinan on tumor growth in murine allogeneic and syngeneic host. *Int J Cancer* 1980a;25:371-6.
9. Zakany J, Chihara G, Fachet J. Effect of Lentinan on the production of migration inhibitory factor induced by syngeneic tumor in mice. *Int J Cancer* 1980b;26:783-8.
10. Mizuno T. The extraction and development of antitumor-active polysaccharides from medicinal mushrooms in Japan [Review]. *International Journal of Medicinal Mushrooms* 1999;1:9-30.
11. Mizuno T. A development of antitumor polysaccharides from mushroom fungi. *Food & Food Ingred J* (Japan). 1996;167:69-85.
12. Kim HW, Kim BK. Biomedicinal triterpenoids of *Ganoderma lucidum* (Curt.:Fr.) P.Karst. (Aphyllophoromycetideae). *International Journal of Medicinal Mushrooms* 1999;1:121-38.
13. Stamets P. *Growing Gourmet and Medicinal Mushrooms*. Berkeley/Toronto: Ten Speed Press; 2000.
14. Chang ST. Mushroom biology: the impact on mushroom production and mushroom products. In: Chang ST, Buswell JA, Chiu SW, *et al*, editors. *Mushroom Biology and Mushroom Products*. Hong Kong: Chinese University Press; 1993. p. 3-20.
15. Hiroshi S, Takeda M. Diverse biological activity of PSK (Krestin), a protein-bound polysaccharide from *Coriolus versicolor* (Fr.) Quél. In: Chang ST, Buswell JA, Chiu SW, *et al*, editors. *Mushroom Biology and Mushroom Products*. Hong Kong: Chinese University Press; 1993. p. 237-245.
16. Mizuno T. The development of an antitumor BRM from song gen, or meshimakobu, *Phellinus linteus* (Berk. et Curt.) Teng mushroom [Review]. *International Journal of Medicinal Mushrooms* 2000;2:21-34.
17. Wasser SP, Weis AL. *Medicinal mushrooms*. In: Nevo E, editor. *Reishi Mushroom* (*Ganoderma lucidum* (Curt.:Fr.) P.Karst.) Haifa, Israel: Peledfus; 1997. p. 1-37.
18. Mizuno T. 2002. Medicinal properties and clinical effects of *Agaricus blazei* Murr. *International Journal of Medicinal Mushrooms* 2002;4 (forthcoming).
19. Mizuno T, Hagiwara T, Nakamura T, Ito H, Shimura K, Sumiya T, Asakura A. Antitumor activity and some properties of water-soluble polysaccharides from "Himematsutake," the fruiting body of *Agaricus blazei* Murrill. *Agricult Biol Chem* 1990;54:2889-96.
20. Ito H, Shimura K, Itoh H, Kawade M. Antitumor effects of a new polysaccharide-protein complex (ATOM) prepared from *Agaricus blazei* (Iwade strain 101) "Himematsutake" and its mechanisms in tumor-bearing mice. *Anticancer Res* 1997;17:277-84.
21. Fujimiya Y, Suzuki Y, Oshiman K, Kobori K, Morigushi K, Nakashima H, Matumoto Y, Takahara S, Ebina T, Katakura R. Selective tumoricidal effect of soluble proteoglucan extracted from the basidiomycete, *Agaricus blazei* Murrill, mediated via natural killer cell activation and apoptosis. *Cancer Immunol Immunother* 1998;46:147-59.
22. Fujimiya Y, Yamamoto H, Niji M, Suzuki I. Peroral effect on tumor progression of soluble beta (1,6)-glucans prepared by acid treatment from *Agaricus blazei* Murr. (Agaricaceae, Higher Basidiomycetes). *International Journal of Medicinal Mushrooms* 2000;2:43-50.
23. Cho SM, Lee Jh, Han SB, Kim BK. Chemical features and purification of immunostimulating polysaccharides from the fruit bodies of *Agaricus blazei*. *Korean J Mycol* 1999;27:170-4.
24. Lorenzen K, Anke T. Basidiomycetes as a source for new bioactive natural products. *Curr Org Chem* 1998;2:329-64.
25. Poppe J. Use of agricultural waste materials in the cultivation of mushrooms. In: Van Griensven DLJL, editor. *Science and cultivation of edible fungi*. Rotterdam/Brookfield: A. Balkema; 2000. p. 3-24.

This novel hat is constructed from the medicinal mushroom known as the Ice Man fungus (*Fomes fomentarius*). In Hungary and the Ukranian part of the Transcarpathian Mountains, large specimens of this fungus grow on European beech trees (*Fagus sylvatica*), and are used to make hats, purses and napkins for decorative purposes. Photo © 2001 Solomon Wasser.

Chaga or cinder conk *Inonotus obliquus* ©2002 Paul Stamets

Eco-labels

May Promote Market-Driven Medicinal Plant Conservation

by Christopher S. Robbins

Issues of quality and sustainable harvest of source plants are increasingly important to the herbal market as consumers evolve in sophistication. Both private and governmental agencies of various interests are working to promote or protect different facets of the environment, production method, or materials. Drawing from standards may lead to a cohesive program to certify the quality of products in commerce, and clearly identify them for market advantage. Several efforts are underway to achieve that end, including a project by TRAFFIC, the wildlife trade monitoring program of the World Wildlife Fund and the World Conservation Union (IUCN).

In August 2001, TRAFFIC surveyed separately two small groups: American consumers and Hong Kong ginseng importers. Both groups expressed their preference for purchasing wildcrafted botanicals that promise higher quality and that are harvested in a matter that promotes environmental quality and protects the future of the species.

The surveys are part of efforts by TRAFFIC North America to improve sustainable production of medicinal plants harvested from the wild. The basis for this work is the belief that market-based strategies for the conservation of medicinal plants may provide the private sector with an economic incentive to contribute to the conservation of these resources, reinforcing or even replacing regulatory intervention. Giving consumers the option to purchase herbal products marketed under a label that reflects sound environmental stewardship is another guiding philosophy.

Under such an "eco-labeling" program, companies would commit voluntarily to buy, manufacture, or sell herbs obtained from sources that have been independently certified by a third-party to meet certain environmental standards, including sustainable harvest levels and practices.[1] In exchange, those companies could use a special label, logo, or seal that allows them to make claims of sustainability and distinguishes their herbal products from market competitors.

The Market Speaks

The results from the survey of American consumers show that most would buy herbal supplements that contain sustainably sourced ingredients, if presented with that choice.

The survey was conducted by Edge Research for TRAFFIC North America in August 2001. Survey respondents were selected from an initial sample of herbal supplement users via the Internet who were subsequently screened and included in the online survey only if they considered themselves the primary shopper within the household. A total of 508 individuals completed the survey. The margin of error was +/- 4.2 percentage points at the 95 percent confidence level.

Using ginseng as a trial case, 78 percent said they would buy ginseng products with labels that verify the sustainability of production instead of those without such a label. Almost 70 percent would still buy "certified sustainable" ginseng even if it meant paying a 5 percent premium. Verifying whether consumers would actually pay more for an eco-labeled product remains to be tested.

To assess the market further, TRAFFIC East Asia distributed an attitudinal survey to 21 ginseng importers based in Hong Kong. The results reveal their concerns about the costs associated with an eco-labeling program for American ginseng (*Panax quinquefolius* L., Araliaceae), but also highlight opportunities for building support for such a program among this group of stakeholders.

Most of the wild American ginseng is exported to and redistributed by traders in Hong Kong, suggesting that the perceptions of this constituency are critical to promoting "certified sustainable" ginseng in the Asian market. Four companies, accounting for approximately one-third of the wild ginseng imported into Hong Kong from the United States, responded to the survey.

The respondents expressed some reservations about the affordability of "certified sustainable" American ginseng, however, they also commented on the inevitability and potential benefits of an eco-label, saying this type of label will likely be implemented in the future and may be useful to prove the authenticity of wild American ginseng to end users.

An interesting finding was the opinion of two of these importers that wild ginseng roots from the United States have been smaller than in previous years and, in their estimation, had decreased in quality. All four respondents ranked size as a critical factor determining quality and price.

Case Study in Ginseng

TRAFFIC selected American ginseng to begin the assessment of the conservation merits of eco-labeling for North American botanicals collected or grown in their natural habi-

tat. Diggers earn an estimated US$18 million annually from the sale of wild American ginseng roots in states where the plant is legally collected.[2] Ginseng (*Panax* spp.) is consistently among the top selling herbs in the American market, with sales in 2001 at nearly US$31 million.[3] This assessment work is part of a broader initiative in which the Yellow Creek Botanical Institute, the Herb Research Foundation, and TRAFFIC seek to foster a sustainable economy in Appalachia by developing, marketing, and managing the region's rich diversity of botanical resources, while striving to protect its natural heritage and environment for future generations.

In 1973, concerns stemming from the harvest of wild American ginseng in the United States and Canada for export to Asian medicinal markets led to its listing in Appendix II of CITES (Convention on International Trade in Endangered Species of Wild Fauna and Flora).[4] Today, the United States is the only exporter of wild American ginseng and implements the CITES listing by authorizing exports on a state-by-state, annual basis depending on the population status of the species and efficacy of management measures in these states.

Ginseng's widespread use affords the species a level of visibility unmatched by any other medicinal plant. Thus, the introduction of an eco-labeled ginseng product into the marketplace may be more recognizable and marketable to consumers than less popular herbs.

In addition, historically steady demand for the valuable wild roots of American ginseng in Asia and potential markets in North America and Europe for sustainably sourced, woods-grown products are likely to provide powerful economic incentives for developing eco-labeling for the species in its natural habitat. The interests of conservationists and Asian traders may merge under eco-labeling, as only the older, more valuable plants would be harvested. Younger plants would be allowed to reach seed-producing age and produce substantive quantities of seed prior to harvest. On the Asian market, the value of a wild American ginseng root is determined primarily by size, with older, larger roots (believed to harbor the highest concentration of active ingredients) fetching the highest prices.[5] One of the most tangible benefits of eco-labeling for traders may be an increase in availability of larger, more desirable roots harvested by wildcrafters or growers who, under the terms of voluntary, third-party certification, would only supply plants meeting minimum age requirements.

Similarly, harvesters and traders are expected to benefit from eco-labeling as Asian buyers begin to associate a "certified sustainable" label with older, larger, and superior wild or woods-grown roots for which they are likely to pay a premium price. Indigenous and local stakeholders, including harvesters and dealers, should and will have a critical role to play in developing an eco-labeling program that reflects their knowledge, use, and management of the resource base.[6]

Claims Aimed At Consumers

American companies are increasingly eager to sell products that claim to contain herbal ingredients that were ethically, sustainably, or ecologically wildcrafted, as evidenced by the number of such claims documented in the marketplace. TRAFFIC's research reveals that more than 100 companies sell botanicals that they claim have been harvested in a responsible manner, but none of these claims is independently substantiated or certified.

Clearly, these claims demonstrate that herbal supplement manufacturers perceive they are catering to a base of consumers who care about the environment and purchase products that conform to their environmental beliefs. Indeed, manufacturers of herbal supplements already procuring raw materials from natural plant populations in a sensitive, sustainable manner may be eligible for third-party certification when or if such a program becomes available.

Work in Progress

Efforts to protect plant resources are not new, neither are they in the hands of just a few organizations. For instance, the Forest Stewardship Council is primarily concerned with the ecological and social criteria of forest products harvest whereas good manufacturing practices (GMPs) place standardization — instead of sustainable sourcing — of ingredients at the top of their priority list. Despite the current emphasis on product standardization, GMPs may be written to take sustainable sourcing into account.

Organic certification, as developed by the U.S. Department of Agriculture's National Organic Program, is another mechanism that supports the sustainable production of "wild crops" and that will allow producers to label wild-harvested plant material as organic.[7]

Still other non-governmental and governmental certification systems for agricultural or forest products are already available to the private sector or are in development.[8] The first phase of TRAFFIC's assessment of eco-labeling for American ginseng is evaluation and comparison of existing certification mechanisms, such as those mentioned above, to determine their strengths, weaknesses, and economic practicality.

Critical to the success of eco-labeling are the opinions and concerns of stakeholders whose input will continue to be sought and integrated into the prioritization and planning process. Pending funding, the next phase of work will focus on the design and implementation of a pilot project, including site selection in western North Carolina and recruitment of landowners, harvesters, traders, and manufacturers to participate in the pilot project.

The results and recommendations from the ginseng case study will be adapted to explore voluntary certification for other medicinal species of commercial value in eco-regions of high conservation importance, such as black cohosh (*Actaea racemosa* L., Ranunculaceae, syn. *Cimicifuga racemosa* (L.) Nutt.) in the Blue Ridge Mountains, Oregon grape (*Mahonia aquifolium* (Pursh) Nutt., Berberidaceae) in the Pacific Northwest, and Asian ginseng (*Panax ginseng* C.A. Mey., Araliaceae) and eleuthero (*Eleutherococcus senticosus* (Rupr. & Maxim.) Maxim., Araliaceae) in the Russian Far East.

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The Road to El Desemboque

by Tim Lowery

We turn off the highway onto a sandy road leading to our destination. Almost wide enough for two cars, the road to El Desemboque snakes its way through the Sonoran Desert. From end to end the *camino* offers stretches of parallel side roads that promise less jarring, dipping, and bouncing than the wash beds and truck ruts of the main road. The truck rattles and squeaks as we traverse a wash. *What am I doing here?* I ask myself. Well, you are here to set up a community pharmacy, study medicinal plants, and encourage traditional foods. *But why are you here?* I brace myself against the dashboard as we blast over a section of rutted roadway. Looking around, I notice the giant saguaros (*Carnegiea gigantea* (Engelm.) Brit. & Rose, Cactaceae) passing by the left and right of the truck. With as many as two dozen arms stretching toward the sky, these ancient beings rise out of the desert and blanket the hillside. Their procession is halted only by the *sierras*, the horizon, and as we draw closer to El Desemboque, the Sea of Cortez. I look towards other plants and try to name those that I've only seen in books. The palo verde (*Cercidium microphyllum* (Torr.) Rose & Johnst., Leguminosae) is green from its pointed tips all the way down until it disappears into the sand. The mighty mesquite (*Prosopis glandulosa* (L. Bens.) M.C. Johnst., Leguminosae) waves gently as we pass. Teddy bear cholla (*Opuntia bigelovii* Engelm., Cactaceae) flaunts its yellow fuzzy nubs, electric against the olive, silver, and taupe of Sonora. I see other smaller brush lining the road that I don't yet recognize, but which I'm certain have medicinal uses.

Medicine. That's why I'm here. I want to see how one small slice of the 80 percent of the world's population who lives without Western pharmaceuticals heals with plants.[1] I want to supplement my pharmacy school education with an experience that may help me understand where medicine came from, where it needs to go, and what I can do to help it get there.

I actually prefer these times when everyone is speaking Seri. They remind me of the connection between language diversity and species diversity, and the knowledge embedded in a language itself.

We round a long curve revealing the cement houses belonging to the Seri residents of El Desemboque. The permanence of these structures reminds me of the importance of the work here. The Seri, or *Comcaac* as they call themselves, lived as hunter/gatherers well into the twentieth century.[2] Settled in the permanent fishing villages of El Desemboque and Puenta Chueca in the middle of that century, the adult population knows a tremendous amount about their desert surroundings. This includes the medicinal plant knowledge their parents depended on. As we pass by the

rows of houses and approach the center of town, these thoughts feed my imagination on the possible impact a community pharmacy could have to help preserve this knowledge.

Tomorrow is July 1, the Seri New Year that celebrates the fruiting season, and the center of town is full of folks preparing for the fiesta. For the next three weeks, I'll live and work with the Seri in El Desemboque, and attempt to set up a community pharmacy using traditional desert medicines for the pharmacopeia. The specifics of how this goal will be accomplished are vague and mysterious, but for today and tomorrow, I am content to enjoy the dancing and feasting during this annual community celebration.

I am here with Laurie Monti, a nurse practitioner, ethnoecologist, and Northern Arizona University professor, who worked with the Seri for five years. The community pharmacy is part of a broader project to promote sustainable desert land use. Laurie will be in El Desemboque for a week, during which time she'll make the necessary arrangements for me to continue working after she leaves.

The author kneels to gather *pechita* near a farm outside of El Desemboque. Photo © 2002 Christina Monroy.

After the New Year's celebration, we meet the women with whom I'll be working. These women are members of Cooperativa Comcaac, a natural products cooperative that promotes traditional foods and medicines. I am most impressed by the age diversity of this group. Ranging from 20 to 60 years old, I view this side-by-side involvement of different generations as a positive sign for the continued transmission of traditional knowledge. Through the course of our conversation, I learn that we won't collect any medicinal plants, as the cooperative already has a good supply. The group wants me to help prepare the collections they already have, including showing them how to make creams and salves. Since now is the prime fruiting season for many species, the women also want to focus on traditional food collections. I run this new information through the objectives list in my head, and find it to match. The role of the pharmacist, my memory tells me, is to provide education about medicines and diseases, ensure proper medication selection, dosage, and dosage form, and encourage the first two components of any chronic disease management plan, proper diet and exercise. Satisfied with the degree of overlap, I respond in my best Spanish, "*Sí, es bueno.*"

I would find it difficult to recommend a better medicine than one that simultaneously promotes health and natural community stewardship.

Pechita, the pod of the mesquite tree, is the first traditional food we collect. Driving into the desert, I follow the directions of one of the cooperative members to a place with *mucho pechita*. Under the shade of a stand of mesquite trees, we gather the ripened pechita that cover the ground. After a little coaching, I begin to distinguish the quality of the pods by taste and thickness. The pods we collect will later be ground into traditional flour and the seeds discarded. For now though, I focus on the task of gathering *pechita*, tasting their hulls for sweetness, and listening to Seri women trade stories in their native tongue.

I actually prefer these times when everyone is speaking Seri. They remind me of the connection between language diversity and species diversity, and the knowledge embedded in a language itself. The Seri give me hope that these people, their way of life, and their surrounding diversity will survive.

Ripe *pitahaya* on an organpipe cactus and the tip of the *palo*, the digging stick used to retrieve them. Photo © 2002 Tim Lowery.

To collect *pitahaya*, the fruits of the saguaro, or organpipe, cactus (*Stenocereus thurberi* (Engelm.) Buxb., Cactaceae), we go further into the desert on side roads and paths I could never navigate on my own. Here we don't have the luxury of mesquite shade and must settle for the small sunless area beneath a saguaro. After placing our lunch and water jugs in this little shaded spot and hanging a colorful scarf to guide us back, we head in different directions carrying *pitahaya* sticks and buckets. The sticks are made from a long saguaro rib with a nail or sharpened stick lashed to one end. Below the point is a v-shaped notch that helps steady the stick against the cactus and provides some leverage for removing stubborn *pitahaya*.

Walking through the dusty wilderness searching for fruiting cactus gives me some sense of how important these traditional food collections are. Not only do they provide the Seri an alternative to a western diet linked to diabetes and obesity, they also strengthen the connection between the Seri and their desert. And this connection has helped the desert remain as it is for as long as it has. I would find it difficult to recommend a better medicine than one that simultaneously promotes health and natural community stew-

ardship.

As we return to El Desemboque shortly after noon, the townspeople emerge from the shade of their homes and congregate by the tailgate of the truck and the buckets of *pitahaya* we are unloading. The sweet, red juice from the fig-like *pitahaya* soon drips from the faces of children and within an hour, the lot is consumed. In the excitement created by this desert treat, sodas and candy are momentarily forgotten.

After *siesta*, I meet with the cooperative to label medicinal plants and to teach some simple cream and salve formulas I learned from herbalist Denise Tracy, founder of The Super Salve Company, prior to my arrival in Mexico. The labels and directions for use have been written in both Seri and Spanish, so the cooperative might sell their herbs to nearby Mexican communities as well as utilize them for the needs of their own tribe. I am concerned primarily with the safety of these herbs and possible contraindications to their use. I had spent some time researching these topics in the U.S. several weeks ago. This proved to be a frustrating endeavor because many of the species in the Seri pharmacopeia had few or no published studies. By now, as I actually work with the Seri, I am content with labels that give the traditional dose and preparation methods, confident that this information would not have been passed down through oral history had they not been safe. Contraindications and interactions with other herbs and drugs, however, still trouble me. How to establish these without knowing the mechanism by which the herbs heal, is a question I'll be thinking about when I return to my formal university pharmacy classrooms.

By now, when I am actually working with the Seri, I am content with labels that give the traditional dose and preparation methods, confident that this information would not have been passed down through oral history had it not been safe.

A sack of *pechita* collected under a stand of mesquite trees near a wash southeast of El Desemboque. Photo © 2002 Tim Lowery.

The women of Cooperativa Comcaac thank me for the help and wave me into the evening. I walk towards the edge of town and down to my camp by the sea. The sky fades over the village, and I think about what I want to do after I leave El Desemboque. Here, in this quiet, distant place, the connection between human health and environmental health is clear. I understand that to promote human health I must also promote the health of the environment. The connection to herbal medicine also comes to mind as healing plants may provide the only sustainable form of medicine.[3] I realize that regardless of the direct implications to the community pharmacy in El Desemboque or elsewhere, I need to learn more about herbal medicine and environmental health. As I lay back on my cot and look out into the stars, the possibilities for service projects that promote health in the broadest sense seem limitless. And perhaps they are.

Tim Lowery is a third-year PharmD. student at the University of North Carolina at Chapel Hill. The funding for his experience was provided by the Joseph Hollingsworth Memorial Scholarship. To contact Tim, please email him at <tlowery@email.unc.edu>.

References:

1. Farnsworth NR, Akerele O, Audrey S, Soejarto DD, Guo Z. Medicinal plants in therapy. *Bull World Health Organ* 1985;63(6):965-1170.
2. Felger RS, Moser MB. *People of the Desert and Sea*. Tucson: University of Arizona Press; 1985.
3. McCaleb RS. Medicinal plants for healing the planet: biodiversity and environmental health care. In: Grifo F, Rosenthal J, editors. *Biodiversity and human health*. Washington DC: Island Press; 1997. p. 221-42.

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consultant to TRAFFIC North America. For additional information on TRAFFIC North America's eco-labeling project, contact the author by email <crobbins@biotaconsulting.com>. To learn more about the TRAFFIC Network's global medicinal plant program and priorities, visit TRAFFIC's website <www.traffic.org>.

References:

1. Bass S, Thorber K, Markopoulos M, Roberts S, Greig-Gran M. Certification's impacts on forests, stakeholders and supply chains. Final report. London: International Institute for Environment and Development; 2001.
2. Robbins, C.S. Ginseng dealers surveyed, conservation measures addressed. *TRAFFIC Bulletin* 1999;18(1):3-5.
3. Blumenthal M. Herb sales down in mainstream market, up in natural food stores. *HerbalGram* 2002;55:60.
4. Robbins CS. Comparative Analysis of Management Regimes and Medicinal Plant Monitoring Mechanisms for American Ginseng and Goldenseal. *Conservation Biology* 2000 October;14(5):1422-34.
5. Persons SW. *American Ginseng: Green Gold*. Revised edition. Asheville (NC): Bright Mountain Books, Inc.; 1986.
6. Turner NJ. "Doing it Right": Issues and Practices of Sustainable Harvesting. (Earlier version presented to Non-Timber Forest Products Workshop, Ktunaxa Kinbasket Treaty Council, Yaqan Nukiy, Creston, B.C.) *B.C. Journal of Ecosystems and Management* 2001;1(1). Online journal <http://www.siferp.org/jem/>.
7. U.S. Department of Agriculture Agricultural Marketing Service. Standards for the National Organic Program in the United States. 2001, Washington, D.C. [cited 2001 Dec 19]. Available online <www.ams.usda.gov/nop>.
8. Ozinga S. Behind the logo, an environmental and social assessment of forest certification schemes. Gerard N, Wenban-Smith J, editors. Fern. United Kingdom; 2001.

Rhodiola rosea
A Phytomedicinal Overview

Photos © 2002
Bertalan Galambosi

by Richard P. Brown, M.D.,
Patricia L. Gerbarg, M.D.,
and Zakir Ramazanov, Ph.D., D.S.

Rhodiola rosea L., also known as "golden root" or "roseroot" belongs to the plant family Crassulaceae.[1] *R. rosea* grows primarily in dry sandy ground at high altitudes in the arctic areas of Europe and Asia.[2] The plant reaches a height of 12 to 30 inches (70cm) and produces yellow blossoms. It is a perennial with a thick rhizome, fragrant when cut. The Greek physician, Dioscorides, first recorded medicinal applications of *rodia riza* in 77 C.E. in *De Materia Medica*.[3] Linnaeus renamed it *Rhodiola rosea*, referring to the rose-like attar (fragrance) of the fresh cut rootstock.[4]

For centuries, *R. rosea* has been used in the traditional medicine of Russia, Scandinavia, and other countries. Between 1725 and 1960, various medicinal applications of *R. rosea* appeared in the scientific literature of Sweden, Norway, France, Germany, the Soviet Union, and Iceland.[2,4-12] Since 1960, more than 180 pharmacological, phytochemical, and clinical studies have been published. Although *R. rosea* has been extensively studied as an adaptogen with various health-promoting effects, its properties remain largely unknown in the West. In part this may be due to the fact that the bulk of research has been published in Slavic and Scandinavian languages. This review pro-

vides an introduction to some of the traditional uses of *R. rosea*, its phytochemistry, scientific studies exploring its diverse physiological effects, and its current and future medical applications.

Rhodiola rosea in Traditional Medicine

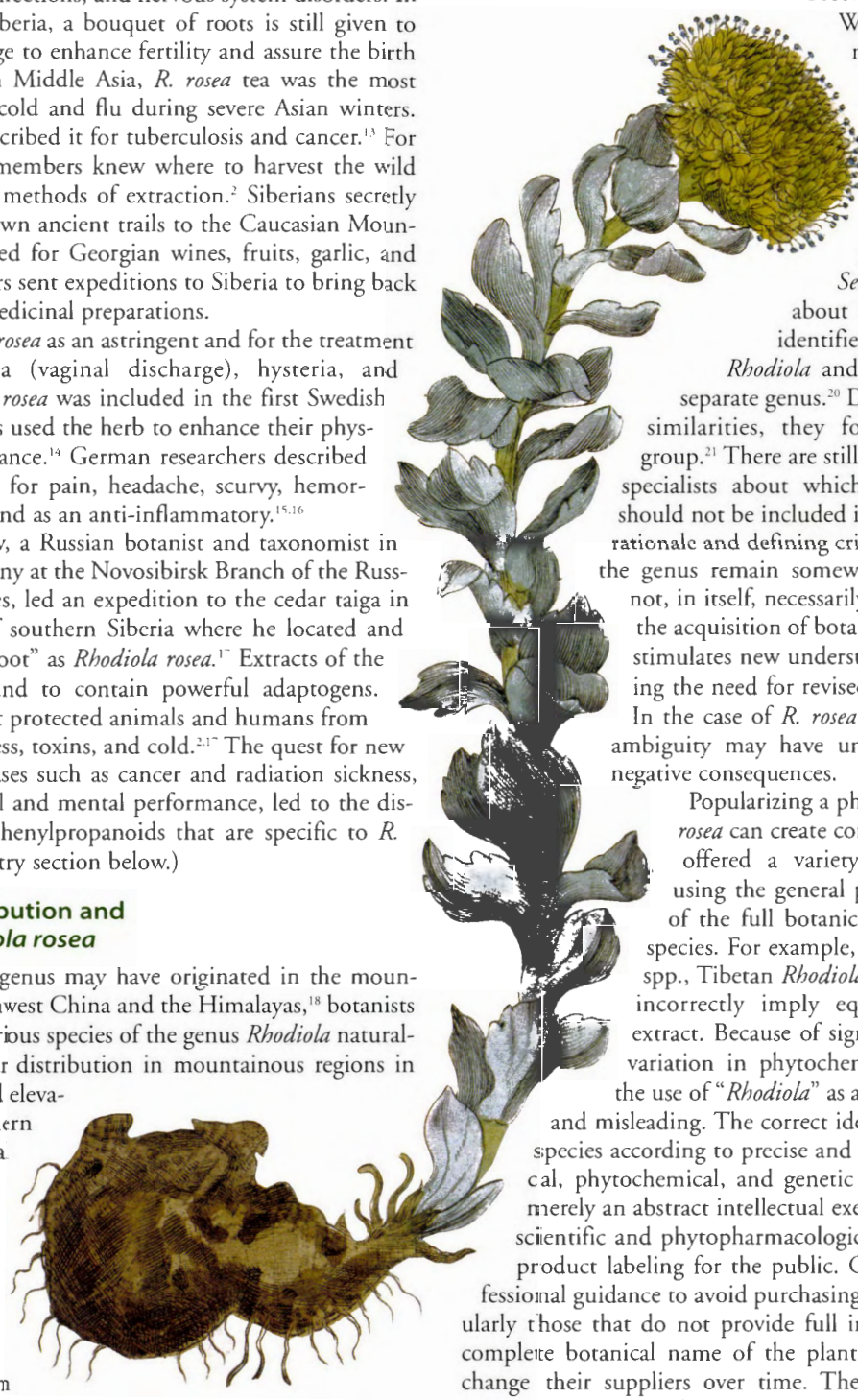
Traditional folk medicine used *R. rosea* to increase physical endurance, work productivity, longevity, resistance to high altitude sickness, and to treat fatigue, depression, anemia, impotence, gastrointestinal ailments, infections, and nervous system disorders. In mountain villages of Siberia, a bouquet of roots is still given to couples prior to marriage to enhance fertility and assure the birth of healthy children.[2] In Middle Asia, *R. rosea* tea was the most effective treatment for cold and flu during severe Asian winters. Mongolian doctors prescribed it for tuberculosis and cancer.[13] For centuries, only family members knew where to harvest the wild "golden roots" and the methods of extraction.[2] Siberians secretly transported the herb down ancient trails to the Caucasian Mountains where it was traded for Georgian wines, fruits, garlic, and honey. Chinese emperors sent expeditions to Siberia to bring back the "golden root" for medicinal preparations.

Linnaeus wrote of *R. rosea* as an astringent and for the treatment of hernia, leucorrhoea (vaginal discharge), hysteria, and headache.[4,7] In 1755 *R. rosea* was included in the first Swedish Pharmacopoeia. Vikings used the herb to enhance their physical strength and endurance.[14] German researchers described the benefits of *R. rosea* for pain, headache, scurvy, hemorrhoids, as a stimulant, and as an anti-inflammatory.[15,16]

In 1961, G.V. Krylov, a Russian botanist and taxonomist in the Department of Botany at the Novosibirsk Branch of the Russian Academy of Sciences, led an expedition to the cedar taiga in the Altai Mountains of southern Siberia where he located and identified the "golden root" as *Rhodiola rosea*.[17] Extracts of the *R. rosea* root were found to contain powerful adaptogens. Research revealed that it protected animals and humans from mental and physical stress, toxins, and cold.[2,17] The quest for new medicines to treat diseases such as cancer and radiation sickness, and to enhance physical and mental performance, led to the discovery of a group of phenylpropanoids that are specific to *R. rosea*. (See Phytochemistry section below.)

Geographical Distribution and Taxonomy of *Rhodiola rosea*

While *Rhodiola* as a genus may have originated in the mountainous regions of Southwest China and the Himalayas,[18] botanists have established that various species of the genus *Rhodiola* naturally display a circumpolar distribution in mountainous regions in the higher latitudes and elevations of the Northern Hemisphere. In Central and Northern Asia, the genus is distributed from the Altai Mountains across Mongolia into many parts of Siberia.[19] According to Hegi, its distribution in Europe extends from Iceland and the British Isles across Scandinavia as far south as the Pyrenees, the Alps, the Carpathian Mountains and other mountainous Balkan regions. Several varieties of *Rhodiola* species have also been identified across Alaska, Canada, and the northern mountains of the continental United States.[20] In fact, the world database of botanical literature shows many citations identifying a broad range of species of the genus *Rhodiola*, in some cases including *R. rosea*, in many diverse locations in northern latitudes (see Table 1).



Rhodiola rosea Baxter, William. *British Phaenogamous Botany*. Oxford, published by the author, sold by J. H. Parker [etc.], 1834-1843, vol. 5, plate 391. Courtesy of The Hunt Institute for Botanical Documentation.

The current taxonomical status of the genus *Rhodiola* has become quite complex. Before World War II, some taxonomists separated different species of *Rhodiola* into an independent genus, belonging to the subfamily *Sedoidae*.[20] Then *Rhodiola* was reclassified as a subgenus of the larger genus *Sedum*, which contained about 10 species. In 1963 Hegi identified more than 50 species of *Rhodiola* and re-established them as a separate genus.[20] Due to their morphological similarities, they form a distinct *Rhodiola* group.[21] There are still differing opinions among specialists about which new species should or should not be included in the genus *Rhodiola*. The rationale and defining criteria for the boundaries of the genus remain somewhat controversial. This is not, in itself, necessarily counterproductive, since the acquisition of botanical knowledge inevitably stimulates new understanding and insight, creating the need for revised systems of classification. In the case of *R. rosea*, however, this taxonomic ambiguity may have unexpected and potentially negative consequences.

Popularizing a phytomedicinal plant like *R. rosea* can create confusion when the public is offered a variety of "*Rhodiola*" products using the general plant family name instead of the full botanical name of the particular species. For example, products called "*Rhodiola* spp., Tibetan *Rhodiola* or Indian *Rhodiola*" may incorrectly imply equivalence with *R. rosea* extract. Because of significant species-dependent variation in phytochemistry and pharmacology, the use of "*Rhodiola*" as a general term is inaccurate and misleading. The correct identification of all *Rhodiola* species according to precise and generally accepted botanical, phytochemical, and genetic taxonomic criteria is not merely an abstract intellectual exercise. It is critical for both scientific and phytopharmacological accuracy, as well as for product labeling for the public. Consumers may need professional guidance to avoid purchasing ineffective brands, particularly those that do not provide full information, including the complete botanical name of the plant species. Companies may change their suppliers over time. Therefore, consumers should periodically check independent sources of product evaluation, as well as requesting information about quality control and content from manufacturers.

The pharmacological and medicinal properties

of *Rhodiola* are species-dependent phenomena.[22] Of all the *Rhodiola* species, *R. rosea* has been the predominant subject of phytochemical, animal, and human studies.[2,18,23,24] Table 2 compares the research record of *R. rosea* with all other species of the genus *Rhodiola*. Approximately 51 percent of all animal studies and 94 percent of all human studies conducted on plants in the genus *Rhodiola* are on the species *R. rosea*. Only *R. rosea* has passed extensive toxicological studies and has been certified safe for both animals and humans.[25]

Table 1. Distribution of plants in the genus *Rhodiola*

Asia: China (Gansu, Hebei, Jilin, Shanxi, Sichuan, Xinjiang); Kazakhstan and Uzbekistan; Mongolia; Russian Federation (Altai, Eastern Siberia, Kamchatka, Khabarovsk, Magadan)

Europe: Austria; Bulgaria; Czechoslovakia; Finland; France; Greenland; Iceland; Ireland; Italy; Norway; Poland; Romania; Russian Federation (European part); Spain; Sweden; United Kingdom; Yugoslavia

North America: Canada (British Columbia, Northwest Territory, Yukon Territory); United States (Alaska, California, Colorado, Idaho, Minnesota, Montana, Nevada, New Mexico, New York, Oregon, Tennessee, Utah, Virginia, Washington, Wyoming)

Phytochemistry of *Rhodiola rosea*

The investigation of the phytochemistry of *R. rosea* root has revealed the presence of six distinct groups of chemical compounds:

- Phenylpropanoids: rosavin, rosin, rosarin (specific to *R. rosea*);
- Phenylethanol derivatives: salidroside (rhodioloside), tyrosol;
- Flavanoids: rodiolin, rodionin, rodiosin, acetylrodalgin, tricin;
- Monoterpernes: rosiridol, rosaridin;
- Triterpenes: daucosterol, beta-sitosterol;
- Phenolic acids: chlorogenic and hydroxycinnamic, gallic acids.

The standardization of *R. rosea* root extracts has gone through two distinct phases. Initially, in the 1970s, the compound responsible for its unique pharmacological properties was believed to be salidroside (rhodioloside).[2,23,24,26,27] Therefore, the first generation of *R. rosea* tincture/extracts approved by the Russian Pharmacopoeia Committee was standardized to a minimum of 0.8 percent salidroside content.[25]

In the late 1980s, demand for *R. rosea*-based phytomedicines dramatically increased. The wild-crafted raw material was overharvested, resulting in a steady decline in the quality and effectiveness of "*Rhodiola*" preparations. Scientific investigation revealed that other species of genus *Rhodiola* (which also contained salidroside) were being substituted for *R. rosea*. While some of these mixed batches were highly variable in quality, others had no pharmacological effect. Logically, the suspicion arose that the salidroside standard was inadequate. Based on comparative analysis, the obvious hypothesis was that the original high potency product contained other active compounds specific to *R. rosea* that had not yet been identified.

Specific compounds set *Rhodiola rosea* apart from other *Rhodiola* species

After more than a decade of research, Kurkin and colleagues presented evidence in 1986 that the chemical composition of *R. rosea* root is, in fact, different from the other species of genus *Rhodiola*.[23] Using newly developed methods of analysis, Dubichev and colleagues demonstrated that *R. rosea* root contains three cinnamyl alcohol-vicianosides — rosavin, rosin, and rosarin — that are specific to this species.[28,29] The term *rosavins* can be used to include rosavin, rosin, and rosarin (see chemical figures).

It became evident that salidroside is present in all chemically analyzed plants in the genus *Rhodiola*, and in a wide variety of species outside the genus.[2,25-34] The term *salidroside* is derived from *Salix*, the genus name for the willows. Salidroside was first isolated in 1926 from *Salix triandra* L. (Salicaceae).[33] Since then it has been detected in *Vaccinium vitis-idaea* L. (Ericaceae) and in *Rhododendron*[35,36] (plants not belonging to the genus *Rhodiola*) in concentrations that can be higher than levels found in *Rhodiola* species, including *R. rosea*. Therefore, salidroside alone is not a useful marker compound for differentiating true *R. rosea* from other *Rhodiola* species; nor should it be used as the only marker compound for the standardization of *R. rosea* root extracts.

According to the revised 1989 Soviet Pharmacopeia,[37] the extracts of *R. rosea* — primarily in the form of water/alcohol tinctures or dried root extract — are now standardized for both rosavins and salidroside. Although rosavins are now the accepted marker for genetically pure *R. rosea* (and its extracts), they are not necessarily the only pharmacologically active ingredients responsible for the efficacy observed in clinical studies. In fact, precise identification of the compounds responsible for the numerous health benefits of *R. rosea* remains to be confirmed.

R. rosea extracts used in most human clinical studies were standardized to minimum 3 percent rosavins and 0.8–1 percent salidroside because the naturally occurring ratio of these compounds in *R. rosea* root is approximately 3:1.

Table 2. Comparison of human and animal studies of plants in the genus *Rhodiola* *

Species name	Animal Studies	Human Studies
R. rosea	32	17
R. alterna	0	0
R. brevipetiolata	0	0
R. coccinea	1	0
R. crenulata	4	1
R. ellipticum	0	0
R. fastigita	2	0
R. gelida	0	0
R. henryi	0	0
R. heterodonta	1	0
R. kirilowii	6	0
R. pinnatifida	1	0
R. quadrifidia	1	0
R. sachalinensis	6	0
R. sacra	5	0
R. wolongensis	1	0
R. yunnanensis	0	0

*NOTE: Numbers in this table indicate the number of animal and human studies on each plant species of the genus *Rhodiola*, according to a Copernic online database search, 2001. This article reviews many additional studies not listed in online databases.

Rhodiola rosea in Modern Medicine

Since 1969, *R. rosea* has been included in official Russian medicine. The Pharmacological and Pharmacopoeia Committee of the Soviet Ministry of Health recommended medicinal use and industrial production of liquid *R. rosea* extract. In 1975, the Soviet Ministry of Health approved and registered preparation No. 75/933/14 as a medicine and tonic, allowing large-scale production under the name Rhodiola Extract Liquid, an alcohol-based extract (40 percent ethyl alcohol). Medical and pharmacological texts describe its use as a stimulant for asthenia (fatigue), for somatic and infectious illnesses, in psychiatric and neurological conditions, and in healthy individuals to relieve fatigue and to increase attention span, memory, and work productivity. The common dose is 5–10 drops 2–3 times a day, 15–30 minutes before eating for a period of 10–20 days. In psychiatric disorders with fatigue, a starting dose of 10 drops 2–3 times a day is gradually increased up to 30–40 drops for 1–2 months.

In Sweden, *R. rosea* was recognized as an Herbal Medicinal Product in 1985 and has been described as an antifatigue agent in the *Textbook of Phytomedicine for Pharmacists*.[9] In the textbook of pharmacology for dispenser training in Sweden, *R. rosea* is mentioned as a plant with a stimulant action. Also, the *Pharmaceutical Book* (*Läkemedelsboken* 97/98) mentions *R. rosea* as one of the most commonly used psychostimulants in the group of officially registered herbal medicinal products.[11] In Denmark, *R. rosea* is registered as a medical product in the category of botanical drugs. Registered preparations are extensively used in Sweden and other Scandinavian countries to increase mental work capacity during stress, as a psychostimulant, and as a general strengthener.

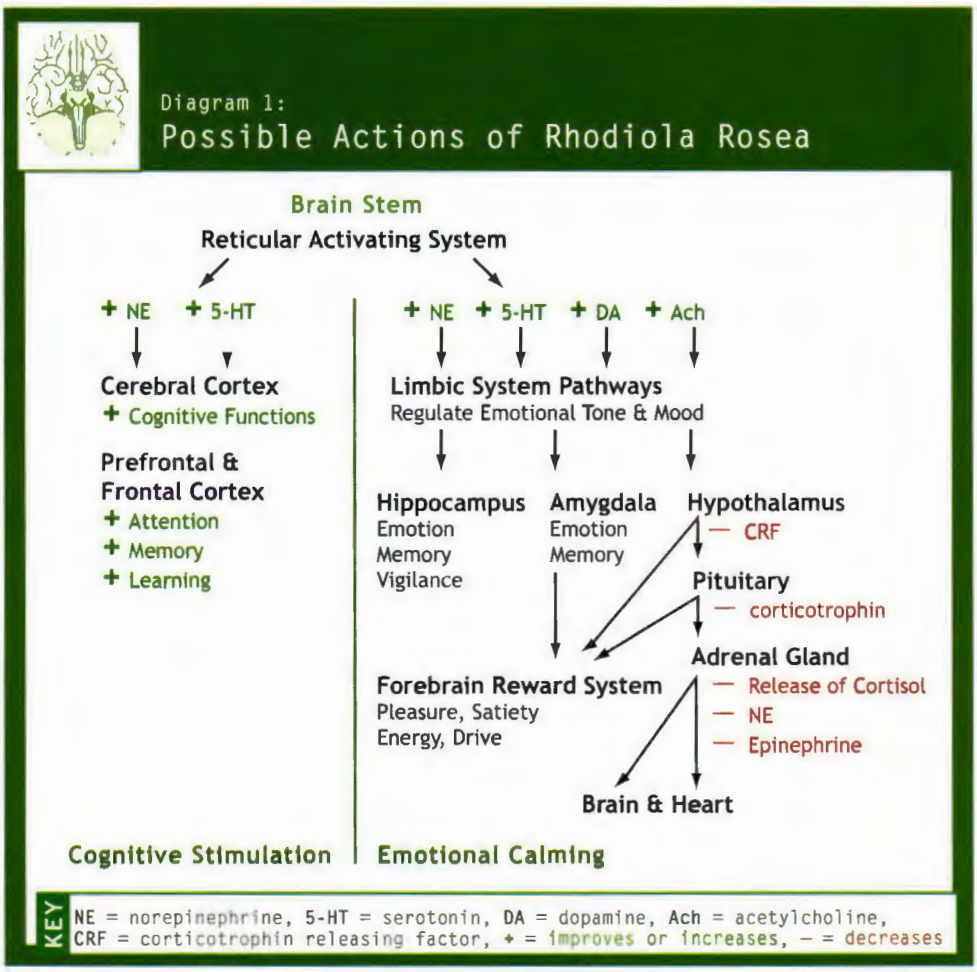
Pharmacological and Clinical Studies

The traditional use of *R. rosea* as a tonic in Siberian and Russian medicine stimulated extensive research leading to identification of *R. rosea* as an adaptogen — a substance that nonspecifically increases the resistance of an organism and does not disturb normal biological parameters. Studies in cell cultures, animals, and humans have revealed antifatigue, anti-stress, antihypoxic (protection against damaging effects of oxygen deprivation), anticancer, antioxidant, immune enhancing and sexual stimulating effects.[2,18,24,38-40] Since the Russian and Bulgarian literature is so extensive, this discussion will highlight seminal studies and major reviews. The authors were fortunate to gain access to original reviews, articles, and doctoral theses. This overview relies heavily on monographs and peer-reviewed publications. The research data contained in these documents are helpful for understanding recent human studies in normal and pathological conditions.

Effects upon the Central Nervous System

The systematic study of the pharmacological effects of *R. rosea*, begun in 1965, found that small and medium doses had a simulating effect, such as lengthening the time mice swim and remain on vertical perches to the limit of their abilities. In contrast, larger doses were found to have more sedative effects. Small doses increased the bioelectrical activity of the brain, presumably by direct effects on the brainstem ascending and descending reticular formation.[23-26,38,39,41] Further studies showed that medium range doses, unlike tranquilizers, enhanced the development of conditioned avoidance reflexes in rats and facilitated learning based on emotionally positive reinforcement.[18,42-46] Overall, in small and medium doses, *R. rosea* stimulated norepinephrine (NE), dopamine (DA), serotonin (5-HT), and nicotinic cholinergic effects in the central nervous system (CNS). It also enhanced the effects of these neurotransmitters on the brain by increasing the permeability of the blood brain barrier to precursors of DA and 5-HT.[2,23,42,46-49]

In comparing studies of *R. rosea*, Asian ginseng (*Panax ginseng* C.A. Mey., Araliaceae), meclofenoxate (centrophenoxine), piracetam, citicholine, and other nootropics (substances that enhance cognition, protect the brain, and have low toxicity and few side effects), Petkov and colleagues noted that all of these agents enhance learning and memory in animal models and increase 5-HT levels in the frontal cerebral cortex.[46-50] Diagram 1 illustrates the possible effects of *R. rosea* on neurotransmitters in multiple neuronal pathways.[51] Starting in the brain stem, *R. rosea* promotes release of NE, 5-HT, and DA in ascending pathways that activate the cerebral cortex and the limbic system.[2,49,50] Consequently, the cognitive (thinking, analyzing, evaluating, calculating, and planning) functions of the



cerebral cortex and the attention, memory, and learning functions of the prefrontal and frontal cortex are enhanced. Other neuronal systems also contribute to the many aspects of memory: encoding, sorting, storage, and retrieval. For example, the cholinergic system uses the neurotransmitter acetylcholine (Ach) and contributes to memory function via pathways ascending from the memory storage systems of the limbic system to various areas of the cerebral cortex (memory retrieval). Agents that block Ach suppress the activity of these ascending pathways and interfere with memory. *R. rosea* reverses this blockade.[49,50] The deterioration of these systems with age results in age-associated memory loss.[52] *R. rosea* may prevent or ameliorate some age-related dysfunction in these neuronal systems.

As an antioxidant,[53-55] *R. rosea* may help protect the nervous system from oxidative damage by free radicals. Stress interferes with memory functions and, over time, causes deterioration in memory systems. In addition to enhancing cognitive functions, learning, and memory by stimulating NE, DA, 5-HT, and Ach neuronal systems, *R. rosea* may exert positive effects on memory and cognition by improving resistance to physical and emotional stress. Thus, the dual action of cognitive stimulation and emotional calming creates benefits for both immediate cognitive and memory performance and for the long-term preservation of brain functions.

The psychostimulant effects of *R. rosea* were studied in 53 healthy subjects and 412 patients with neuroses and asthenic syndromes (of both functional and organic origin).[56-58] Symptoms of asthenia (fatigue, decline in work capacity, trouble falling asleep, poor appetite, irritability, and headaches) responded favorably to *R. rosea* 50 mg three times a day. Treatment durations ranged from 10 days to 4 months. The asthenic states included both psychiatric and physical causes, for example, following influenza or other illness. In an open study of 128 patients aged 17–55 years, *R. rosea* alleviated fatigue, irritability, distractibility, headache, weakness and other vegetative symptoms in 64 percent of cases.[57] Improvement was assessed by psychological testing and work productivity.

In 1869 Beard coined the term "neurasthenia" to include various forms of nervous asthenia. Controversy over this term has centered on the overlap of symptomatology and co-morbidity with other conditions (e.g., depression, neuroses, somatoform disorders, and chronic fatigue syndrome). Although this diagnosis has fallen out of favor in the United States and no longer appears in *The Diagnostic and Statistical Manual of the American Psychiatric Association* (DSM-IV),[59] it is still widely used throughout the world.[60-63] Neurasthenia is defined by the World Health Organization in the *International Classification of Diseases* (ICD-10)[64] as:

- either persistent and distressing feelings of exhaustion after minor mental effort, or persistent and distressing feelings of fatigue after minor physical effort;
- accompanied by one or more of the following symptoms: muscular aches or pains; dizziness; tension headaches; sleep disturbance; inability to relax; and irritability;
- inability to recover through rest, relaxation, or enjoyment;
- does not occur in the presence of organic mental disorders, affective disorders or panic, or generalized anxiety disorder.

In an open study 27 healthy students, physicians, and scientists aged 19–46 years were given 10 drops of *R. rosea* tincture (equivalent to 100–150 mg *R. rosea* extract) once or twice a day for 2–3 weeks, beginning several days before intense intellectual work, such as final exams.[58] The extract improved the amount and quality of work and in all cases prevented asthenic decompensation (loss of work capacity due to fatigue). A series of studies using a proofreading test showed that a one-time dose of *R. rosea* did not significantly increase the number of symbols corrected, but very significantly decreased the percent of errors made, particularly over an 8-hour period.[65,66] Positive results found in the studies of proofreading tests were based on 300 mg/day or more. In medical treatments, the usual doses are 200–600 mg/day. *R. rosea* increased intellectual capacity (particularly by improving perception and processing of information) to a greater degree than an extract of eleuthero, formerly called Siberian ginseng (*Eleutherococcus senticosus* Rupr. et Max., Araliaceae).[18]

The decrease in physical and mental performance of physicians on prolonged night call is well known. Low dose (170 mg/day) *R. rosea* extract was given to 56 young, healthy physicians on night call.[18] The effect was measured as total mental performance calculated as "Fatigue Index." The tests reflected an overall level of mental fatigue involving complex cognitive functions, such as associative thinking, short-term memory, calculation, concentration, and speed of audio-visual perception. These parameters were tested before and after night duty during three periods of two weeks each in a double-blind crossover trial. A statistically significant improvement in mental performance tests was observed in the treatment group (*R. rosea*) during the first two-week period. However, at 6 weeks the effect appeared to be lost. No side effects were reported. These results suggest that *R. rosea* extract can reduce fatigue under certain stressful conditions for some period of time. Possible reasons for the loss of efficacy over time may be the low dose used, the crossover design, or the overall length of night duty with increased fatigue by weeks 5 and 6.

Spasov and colleagues compared 100 mg/day *R. rosea* extract (SHR-5, Swedish Herbal Institute, Goteborg, Sweden; standardized to 3 percent rosavin and 0.8 percent salidroside) with placebo in a double-blind 20-day study of 60 Indian medical students studying in Russia during their final exam period.[38] Despite the low dosage, investigators found significant improvements in general well-being, physical fitness, mental fatigue, final exam grades, and coordination, but not in some aspects of cognitive functioning in students taking *R. rosea* extract compared to placebo.

In a double-blind placebo-controlled study of 60 foreign students at a Russian high school, administration of a *R. rosea* extract (660 mg/day of a preparation named Rodaxon) resulted in an increase in physical (velergometric) work capacity, coordination, kinesthetic sensitivity, and general well-being along with a decrease in psychic fatigue and situational anxiety.[39] Unfortunately, this study provides no information on the amount of *R. rosea* in the Rodaxon preparation.

R. rosea was beneficial in posttraumatic and vascular lesions of the brain. It was especially effective in combination with piracetam for patients with marked cognitive dysfunction.[56] However, it did not reduce manic symptoms and could worsen paranoid states. In one study of more clearly depressed patients, *R. rosea* in combination with tricyclic antidepressants (TCAs) produced significant improvement in the majority of cases and decreased side effects of the TCAs.[67] Ultimately, some of these patients were able to respond to *R. rosea* alone.

Antipsychotic medications used in large doses over many years to treat schizophrenic patients sometimes affect the dopaminergic nerves in the basal ganglia, the same nerves that are damaged in patients with Parkinson's Disease. When these nerves are compromised, patients develop a constellation of "Parkinsonian" symptoms, including stiffness, tremors, bradykinesia (slowed movements), and others. Anticholinergic medications have been used to relieve these symptoms when they are caused by antipsychotic medication; however, they sometimes fail to help. In schizophrenic patients whose anticholinergic medications had failed to relieve Parkinsonian symptoms, *R. rosea* was found to be of benefit.[56,68]

R. rosea may affect emotional tone by influencing neurotransmitter monoamine levels (NE, DA, 5-HT) in nerve tracts involved in the regulation of mood, anxiety, and emotion in the amygdala, hippocampus, hypothalamus, and midbrain. The stimulation of nicotinic cholinergic activity in the emotional circuits of the limbic system (in the temporal lobe) may also contribute to these effects. Alterations in monoamine levels underlie this complex spectrum of psychotropic activity: stimulating, tranquilizing, anti-stress, and antidepressant.

The authors have found that *R. rosea* can help patients with depressive syndromes, mental and physical fatigue (secondary to psychiatric and medical conditions), memory loss and cognitive dysfunction from a variety of causes, sexual dysfunction, and menopausal-related disorders. Dr. Brown and Dr. Gerbarg have successfully treated more than 150 individuals with *R. rosea* extract (3 percent rosavin and 1 percent salidroside) and have supervised the treatment of more than 100 additional cases (See Case Studies).

Effects on Physical Work Capacity

A number of studies have shown that *R. rosea* increased physical work capacity and dramatically shortened the recovery time between bouts of high-intensity exercise. These studies included normal individuals exposed to maximal work on a bicycle ergometer and Olympic-level cross country skiers and biathletes.[69] In one study, 52 men (18–24 years of age) were given one dose of either 15 drops of *R. rosea* extract, 2 ml eleuthero, or 1 ml of a 1 percent solution piridrol (a stimulating psychotropic similar to methylphenidate). Fifteen drops of *R. rosea* extract is approximately equivalent to 150 mg of dry encapsulated root extract standardized to 3 percent rosavin and 1 percent salidroside. After 30 minutes, they pedaled an electric bicycle ergometer to produce a precise amount of work-induced baseline fatigue. After a 5-minute rest, they performed further work to determine the maximal duration of work they could accomplish at a specific intensity. During the second period of work, *R. rosea* drops, eleuthero extract, and piridrol increased work capacity by 9 percent, 6 percent, and 6 percent respectively ($p<0.04$) compared to placebo controls. Recovery was defined by the time of normalization of heart rate and arterial pressure. During the recovery period, at 10 minutes, the pulse slowed by a factor of 2.5 (67 beats per minute) in the *R. rosea* group versus 1.9 (87 beats per minute) in the control group. During the 3-day total recovery period, subjects given piridrol complained of insomnia, excitability, and irritability; whereas those given *R. rosea* had no adverse side effects and no complaints.

Endurance is the capacity to maintain work despite fatigue. Forty-two master level competitive skiers (20–25 years of age) took either *R. rosea* extract or placebo 30–60 minutes before training races (30 km) and a biathlon (20 km race on skis carrying a rifle and shooting targets at stops). Athletes given *R. rosea* had statistically significant increased shooting accuracy, less arm tremor and better coordination. Thirty minutes after work performance, the heart rate in the *R. rosea* group was 104–106 percent of baseline, versus 128.7 percent in the placebo group ($p<0.02$). *R. rosea* improved recovery time, strength, endurance, cardiovascular measures, and coordination.[69]

Adaptogens differ from other stimulants during forced, exhaustive muscular work. With classical stimulants the initial increase in work-capacity is followed by a period of substantially decreased (markedly below average) work-capacity. Repeated use of CNS stimulants depletes brain catecholamines and decreases conditioned reflexes. In contrast, with extracts of *R. rosea*, the initial increase in work-capacity is followed by a lesser diminution, such that the work-capacity continues to be above average.[70]

Animal studies suggest mechanisms that may be involved in these effects. *R. rosea* increased essential energy metabolites, adenosine triphosphate (ATP), and creatine phosphate in the muscle and brain mitochondria in mice made to swim to their limit.[71] It may also enhance the ammonia reassimilation and energy metabolism of the cell by increasing ATP, ribonucleic acid (RNA), protein, and amino acid synthesis.[72] In animal studies, *R. rosea* increased metabolism of fats twice as much as eleuthero[73] and improved energy metabolism in the brain during intensive muscular workloads.[74]

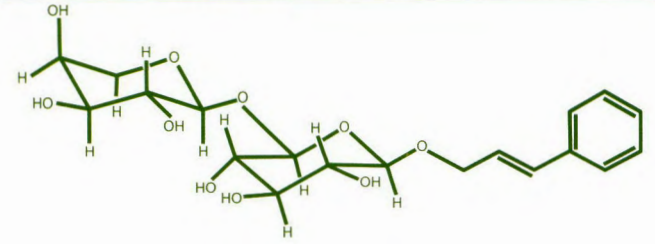
Above and left: ***Rhodiola rosea*** Oeder, G. C. [Flora Danica.] Icones plantarum sponte nacentium in regnis Daniae et Norvegiae ... Hafniae, C. [& A.] Philibert, 1766 [i.e., 1761]-1883, vol. 2, plate 183. Courtesy of The Hunt Institute for Botanical Documentation.

Adaptogenic, Anti-Stress, and Neuroendocrine Effects

In their classic 1968 paper, Soviet pharmacologists Brekhman and Dardymov surveyed the literature on 189 medicinal plants and identified five (including *R. rosea*) that met the three defining criteria for an adaptogen:[75]

- An adaptogen should be innocuous and cause minimal disturbance of the normal physiological functions of an organism;
- The action of an adaptogen should be nonspecific (i.e., it should increase resistance to adverse influences of a wide range of harmful factors of physical, chemical, and biological nature);
- An adaptogen may possess normalizing action irrespective of the direction of the preceding pathological changes (i.e., if a body parameter is high, the adaptogen brings it down towards normal; if a parameter is low, the adaptogen brings it up towards normal).

Figure 1: Rosavin

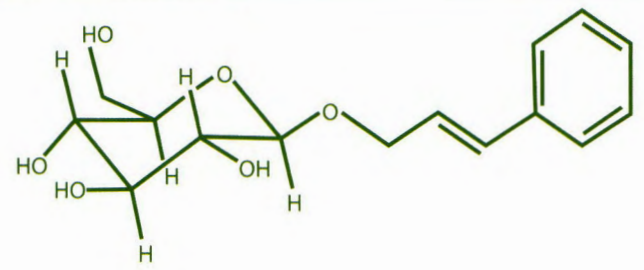


The forced swimming test, used by Russian scientists to measute nonspecific resistance to stress, was later named after Porsolt who assigned specific parameters such as water temperature and the dimensions of the glass cylinder in which a mouse or rat was forced to swim to exhaustion (about 15 minutes). After an initial period of vigorous activity, the rodent adopts a characteristic immobile posture, making only the minimal movements necessary to stay afloat.[76] The validity of the Porsolt swim test and its relationship to depression have been discussed extensively[77,78] and it subsequently became a screening test for antidepressant agents by pharmaceutical companies. Although different laboratories have made minor technical modifications, the fundamentals of the test remain the same. Adaptogens and antidepressants increase the amount of time the animal is able to keep swimming actively.[75] Panossian and colleagues propose to update the definition of adaptogen by highlighting more specific biochemical actions as metabolic regulators.[70] The wide range of medical benefits and physiological actions may be based on the effects of adaptogens on regulatory systems found in many organs and tissues (e.g., immune, hormonal, CNS, cardiovascular, muscular, etc.). They hypothesize that adaptogens reduce damage from stressors by altering the reactivity of the organism's defense system, including the hypothalamic pituitary axis (HPA) and the efferent sympatho-adrenal system (SAS).[70]

A recent study showed that *R. rosea* and eleuthero protected the embryos of freshwater snails (*Lymnaea stagnalis*) from a variety of environmental stressors.[79] Enhancement in resistance was studied by applying phyto-adaptogen extracts for a period of 20 hours to 3-day old *L. stagnalis* larvae. Subsequently the larvae were exposed to the following highly toxic environmental stressors: a physical stress (heat shock: 43 degrees C for 4 minutes); an oxidative stress (superoxide radicals induced by menadione 600 microM for 2 hours); and heavy metal-induced stress (copper 50 microM for 1 hour or cadmium 20 microM for 1 hour). Both eleuthero and *R. rosea* strongly protected snail embryos from lethal heat shock, from the adverse effects of menadione-induced superoxide radicals, and from toxic exposure to heavy metals (copper and cadmium). Although the degree to which resistance was enhanced depended on the type of stressor applied, these results confirm the definition of phyto-adaptogens as being universal enhancers of non-specific resistance against different kinds of stress conditions. The mechanisms of nonspecific resistance are not entirely clear, but probably involve improvements in cellular energy metabolism, based in part on ATP (as discussed above).

In higher animals and humans, nonspecific resistance may also be enhanced by improvements in the neurological mechanisms of dealing with stress (catecholamines, serotonin, and endorphins). The serotonin system is necessary for the stress response reaction, adaptation to new environmental conditions, and tolerance of hypoxia. Numerous stressors decrease serotonin in the hypothalamus. Theoretically, the ability of *R. rosea* to increase the nonspecific resistance of animals may be related to its capacity to increase serotonin in the hypothalamus and midbrain. Additional research showed that an intact hypothalamic pituitary adrenal axis and participation of the gonads and thymus were necessary for this antistress effect.[2] Furthermore, *R. rosea* reduces the activation of several components of the stress response system. For example, it modestly increased serum beta-endorphins that protected rats against subsequent stress-induced excess endorphin elevation.[80] In addition, *R. rosea* moderates the release of opioid peptides that occurs as part of the pituitary adrenal axis response to stress. This reduced release protects against sudden excess opioid and catecholamine (NE and DA) levels (which interfere with normal brain functions and can lead to heart damage), while allowing a more moderate release that increases stress tolerance without damaging the central nervous system or the cardiovascular system (see Diagram 2). *R. rosea* extracts also protect the brain and heart by reducing the secretion of corticotrophin releasing factor (CRF) under stress.[80,81]

Figure 2: Rosin



Endocrine and Reproductive Effects

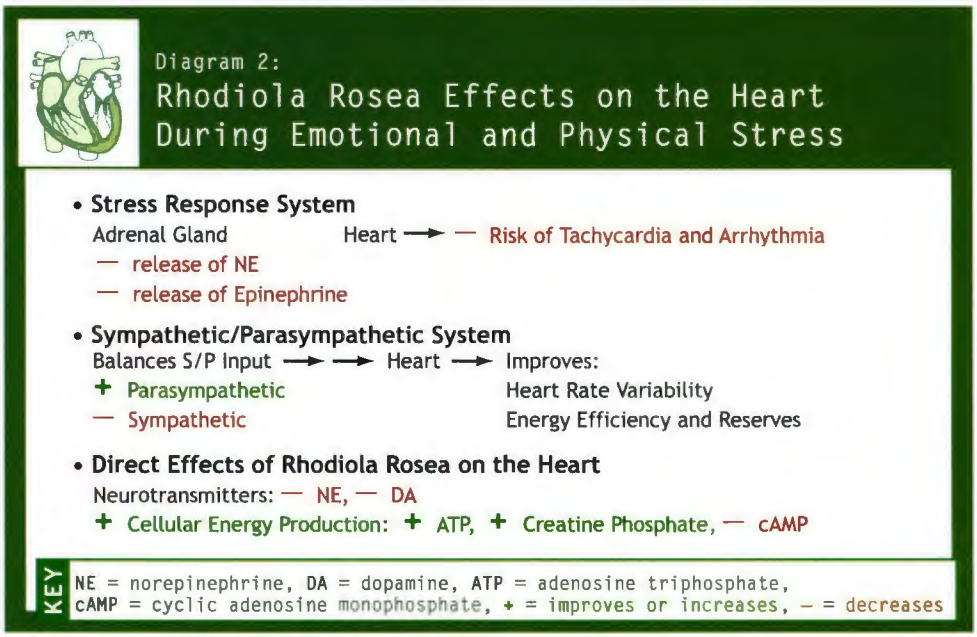
Neuroendocrine animal studies showed that *R. rosea*, like other adaptogens, enhanced thyroid function without causing hyperthyroidism.[81] In addition, the thymus gland functioned better and was protected from the involution that occurs with aging. The adrenal glands functioned with better reserve and without the kind of hypertrophy caused by other psychostimulants.

Egg maturation was enhanced in rats and an anabolic effect in males (increased muscle building and gonad strengthening similar to effects of low-dose testosterone) was observed in a number of

species. Administration of rhodosin (extract of *R. rosea* for intravenous, intramuscular, or peritoneal injection) to sexually mature female mice over a period of 4 weeks prolonged menstruation from 1.3 days (control) to 2.8 days (rhodosin treated), reduced the resting period from 3.8 days (control) to 2.2 days (rhodosin treated), and increased the relative number of estrus days from 29 percent to 56 percent. In the majority of rhodosin treated animals, the number of growing follicles, the oocyte volumes, the accumulation of RNA in oocyte cytoplasm, the proliferation of the lining and glandular cells of the uterine horns, and the preparation of uterine mucosa for fertilization all increased. In sexually mature mice, rhodosin increased the mean weight of the uterine horns from 39.6±4.11 mg to 59.5±1.59 mg and the mean weight of the ovaries from 6.4±0.65 mg to 9.1±0.45 mg. However, the administration of rhodosin to sexually immature female white mice for 3 weeks did not affect sexual maturation, the onset of estrus, the weight of ovaries or uterine horns, or the maturation of follicles. Thus, it is probable that the estrogenic effects of *R. rosea* preparations depend upon a specific hormonal milieu.[82,83]

These pre-clinical investigations led to a study of *R. rosea* extract in women suffering from amenorrhea (loss of menstrual cycles). Forty women with amenorrhea were given *R. rosea* (either 100 mg *R. rosea* extract orally twice a day for 2 weeks, or 1 ml rhodosin intramuscularly for 10 days). In some subjects the treatment cycle was repeated 2–4 times. Normal menses were restored in 25 women, 11 of whom became pregnant. In those with normal menses, the mean length of the uterine cavity increased from 5.5 cm to 7.0 cm (normal) after *R. rosea* treatment.[82,83] One of the authors (Dr. Brown) has treated in his practice several women who had failed to conceive with standard fertility drugs, and who become pregnant within several months of beginning *R. rosea* extract. These preliminary clinical observations warrant controlled follow-up clinical trials. Using the *in vitro* estrogen receptor competition assay, Patricia Eagon, Ph.D. (personal communication, December 2001) recently found that *R. rosea* extract showed strong estrogen binding properties that require further characterization.

In an open study, 26 out of 35 men with erectile dysfunction and/or premature ejaculation (of 1–20 years duration) responded to *R. rosea* (150–200 mg/day for 3 months) with substantially improved sexual function, normalization of prostatic fluid, and an increase in 17-ketosteroids in urine.[56,69]



Cardioprotective Effects

Cardioprotective effects of *R. rosea* include: prevention of stress-induced cardiac damage,[80,81,84] decreased myocardial catecholamines and cyclic adenosine monophosphate (cAMP) levels; and reduced adrenal catecholamine release[80,81] (see Figure 2). Furthermore, *R. rosea* activation of mu-opiate receptors in heart muscle prevented reperfusion arrhythmias in animal hearts. This effect could be blocked by naloxone injection (known to inhibit mu-opiate receptors), thus confirming that the anti-arrhythmic effect of *R. rosea* is associated with the mu-opiate receptors in myocardial (heart) muscle.[84]

In a series of joint Swedish and Russian double-blind, randomized placebo-controlled studies,[85] 10 healthy but sedentary men (ages 20–31 years) were evaluated. Twenty percent of the subjects had average physical work capacity as measured by Power Work Capacity (PWC-170) and 80 percent had below-average PWC-170, indicating a low level of physical training (PWC-170 is a calculation based on the amount of work performed by a man if his heart rate reaches 170 beats per minute, bpm). A sequence of complex 1- to 7-day trials compared the effects of an adaptogen formula, a mixture of mono- and polyphenolic adaptogens (MMPA). Each tablet contained the following ingredients: 3 mg rhodioloside from *R. rosea* root extract, 50 mg; 3 mg total sum of isofraxidine-, syringine-, and syringaresinoie-glycosides from eleuthero root extract, 100 mg; and 4 mg schizandrine and gamma-schizandrine from schisandra (*Schisandra chinensis* (Turcz.) Baill., Lamiaceae) fruit extract, 150 mg.

During the 7-day adaptogen trial, subjects were given 3 capsules (containing a total of 150 mg *R. rosea*) twice a day on days 1–3; 4 capsules (200 mg *R. rosea*) twice a day on days 4–6, and 4 capsules once on day 7. The mean increase in physical work capacity was 28 percent with dosed physical loads in subjects treated with the adaptogen formula. Thus, sedentary subjects given the adaptogen were able to perform in the lower level of trained athletes without any exercise training. Their heart rate variability and inotropic (strength of heart muscle contractility) functions improved.

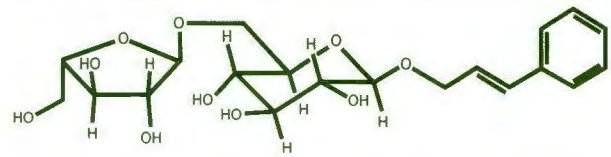
Both the sympathetic and parasympathetic inputs to the heart were enhanced such that the heart showed increased reserves under stress of greater intensity. The autonomic nervous system controls automatic or involuntary functions of the body. It has two components: the sympathetic and the parasympathetic nerves (see Diagram 2). The sympathetic nervous system is the "fight-or-flight" system that helps the organism respond to stress (e.g., by increasing heart rate, respiratory rate, and muscle tone). The parasympathetic nervous system conserves and restores energy (e.g., by slowing the heart rate, respiratory rate, and metabolism). By enhancing the

functions of the sympathetic and parasympathetic systems, *R. rosea* enables the organism to put out more energy during stress while at the same time maintaining higher energy reserves. One of the challenges presented by research on a multi-ingredient formula is that it is not usually possible to attribute the results to the activity of any one single herbal component. However, the results of this study are consistent with results of other research conducted solely on *R. rosea* monopreparations.

Antioxidant and Anti-carcinogenic Effects

R. rosea is rich in phenolic compounds, known to have strong antioxidant properties.[53,86] Animal studies have shown that *R. rosea* decreases toxicity from cyclophosphamide, rubomycin, and adriamycin (anti-cancer drugs), while it enhances their anticarcinogenic effects.[87-89] Udintsev and Schakhov studied the effect of *R. rosea* root extract (RRRE), a tincture manufactured according to the Russian Pharmacopoeia standards (minimum 0.8 percent salidroside and 3 percent rosavin), on tumor cells (transplanted into mice) and normal bone marrow cells in two mouse cancer models.[90] One group of mice with Ehrlich ascites tumor (EAT) and another group with Lewis lung carcinoma (3LL) were first treated with 100 mg/kg cyclophosphamide (a chemotherapy agent) that suppressed tumor growth to 31–39 percent and limited 3LL

Figure 3: Rosarin



metastases to 18 percent, while also reducing the number of normal bone marrow cells, leucocytes, and myelokariocytes, to 40–50 percent and 20–25 percent of normal, respectively. In comparison, RRRE, 0.5 mg/kg/day given orally 2–8 days after tumors had been transplanted, suppressed growth of both tumors by 19–27 percent and 3LL metastases 16 percent. However, in contrast to cyclophosphamide, RRRE caused no reduction in normal bone marrow

Clinical Case Studies

The following cases are representative examples of the many clinical situations in which *R. rosea* may be beneficial. Although the presentation of individual cases does not carry the weight of double-blind placebo-controlled trials, the authors hope that these samples from their larger case series may help to generate interest and funding for future controlled clinical trials to explore the medical applications of this multipotent medicinal herb. Note that in some cases the patients served as their own controls by discontinuing *R. rosea*, relapsing, and then improving upon resumption of treatment.

Ms. W., a 45-year-old writer, never quite finished her doctoral thesis. A "block" prevented her from completing any manuscripts for publication. Seven years of psychotherapy did not alleviate the problem. After "drifting" for years and being terrified of taking any more prescription antidepressants, she tried 100 mg extract of *R. rosea* (Rosavin™, a preparation standardized to 1 percent salidroside and 3 percent rosavin, Ameriden International, Fallbrook, CA) twice a day. Although she had not considered herself to be depressed (and did not meet criteria for dysthymic disorder), within 6 weeks she experienced a new sense of enthusiasm and increased productivity. She became able to complete writing projects and to feel happy with herself. She was well for over two years on *R. rosea*. However, feeling recovered and happily married, she decided on her own to stop the herbal medicine and gradually relapsed over 6 months. Upon resuming the *R. rosea*, she again improved with full recovery.

Ms. P., a 50-year-old computer analyst, complained of constant fatigue, dragging herself out of bed every morning, and dreading encounters at work. Because she was highly sensitive to side effects of any psychotropic medication, she began with one pinch (equivalent to about 50 mg) of *R. rosea* extract (Rosavin™) in her morning tea. Within a few days her fatigue was gone. She had the energy and confidence to deal more effectively with the inevitable conflicts at work.

Ms. B., a 45-year-old mental health professional, had refractory depression and fibromyalgia for 5 years. Her symptoms were completely unresponsive to multiple trials of psychotropic medication. She had a partial response to the antidepressant sertraline (Zoloft®, a selective serotonin reuptake inhibitor, SSRI), but this was not adequate for her to do more than carry out her daily job. The addition of 600 mg/day *R. rosea* extract (Rosavin™) enabled her to return to normal enjoyment and full productivity in life. It took about 2 months to see these effects. After 6 months, the patient began to doubt that she needed the *R. rosea* and discontinued it on her own, only to relapse over the next 3 weeks. Upon reinstitution of the *R. rosea*, she returned to full remission and remains well 2 years later on sertraline and *R. rosea*.

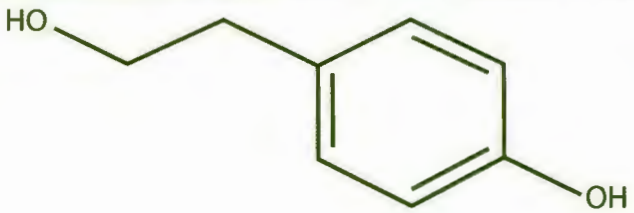
Mr. S., a 74-year-old man, had suffered from Parkinson's disease for 10 years. Despite conventional treatment with pramipexole (Mirapex®), levodopa/carbidopa (Sinemet®), donepezil (Aricept®), and rivastigmine (Exelon®) for motoric and cognitive deficits, he was functioning poorly. He spent most of the day sitting in a chair, rarely speaking or initiating any activities. His wife, a practicing neurologist, carefully observed his clinical status and reported that within one week of starting 300 mg *R. rosea* extract (Rosavin™) twice daily he began to recover with marked progressive improvements in his abilities to think, speak, read, and initiate independent activities. Because of some residual cognitive impairment, galanthus (*Galanthus* spp., Amaryllidaceae) an herbal extract (customized formula by Ameriden International containing 100 mg *R. rosea*, 200 mg galanthus, and 50 mg plant cell-derived vitamin C) was added with consequent additional improvement.

Ms. A., an athletic 62-year-old Oriental woman, was diagnosed with infiltrating ductal carcinoma of one breast. She began chemotherapy but suffered extreme fatigue and suppression of her white and red blood cell counts to the point where, despite conventional treatment adjuvants, the chemotherapy regimen had to be repeatedly interrupted. A trial of 150 mg *R. rosea* extract (Rosavin™) twice daily restored her energy and completely normalized her white and red blood cell counts, allowing completion of chemotherapy. Four months after mastectomy and chemotherapy, Ms. A. resumed her usual rigorous martial arts practice.

cells. In animals given both RRRE and cyclophosphamide, the RRRE increased the antimetastatic effect of cyclophosphamide by 36 percent ($p<0.05$). RRRE also increased the number of leukocytes by 30 percent and myelokariocytes by 16–18 percent.

In another mouse tumor model, Udintsev and colleagues showed that RRRE (minimum 0.8 percent salidroside and 3 percent rosavin) increased the antitumor effect of the drug adriamycin while substantially reducing its liver toxicity.[89] Many chemotherapy agents are hematotoxic (reduce the number of normal blood cell precursors in bone marrow) or hepatotoxic (cause damage to the liver). These serious side effects were significantly ameliorated by RRRE. Thus, the research suggests that RRRE can both enhance tumor inhibition by chemotherapeutic drugs while alleviating dangerous side effects.

Figure 4: Tyrosol



Substances that reduce the incidence of chromosomal aberrations are termed antimutagenic. Salikhova and colleagues found that in mice injected with cyclophosphamide, RRRE (minimum 0.8 percent salidroside and 3 percent rosavin) had antimutagenic effects.[91] Compared to placebo controls, RRRE reduced the development of chromosomal aberrations by 50 percent and reduced the incidence of cells with micronuclei by more than 50 percent. RRRE also increased indices of DNA repair in bone marrow cells after exposure to the mutagen N-nitroso-N-methylurea (NMU).[91]

In a small pilot study of 12 patients with superficial bladder carcinoma (TIG1-2), treatment with RRRE (minimum 0.8 percent salidroside and 3 percent rosavin) improved parameters of leukocyte integrines and T-cell immunity.[92] The average frequency of relapse was reduced, but did not reach statistical significance. Larger placebo-controlled studies of *R. rosea* extracts to augment tumor inhibition and reduce toxic effects of chemotherapy agents are needed.

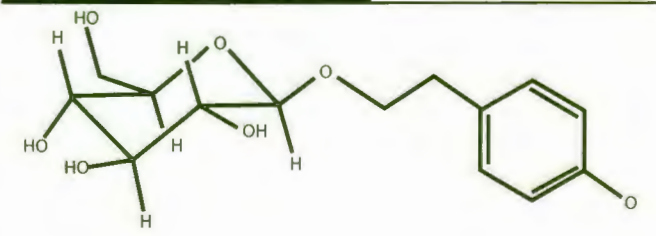
Toxicity, Side Effects, and Contraindications

R. rosea has a very low level of toxicity. In rat toxicity studies, the LD_{50} (lethal dose at which 50 percent of animals die) was calculated to be 28.6 ml/kg, approximately 3,360 mg/kg.[25] The equivalent dosage in a 70 kg man would be about 235 gm or 235,000 mg. Since the usual clinical doses are 200–600 mg/day, there is a huge margin of safety.[87]

Overall, *R. rosea* has very few side effects. Most users find that it improves their mood, energy level, and mental clarity. Some individuals, particularly those who tend to be anxious, may feel overly activated, jittery, or agitated. If this occurs, then a smaller dose with very gradual increases may be needed. *R. rosea* should be taken early in the day because it can interfere with sleep or cause vivid dreams (not nightmares) during the first few weeks. It is contraindicated in excited states. Because *R. rosea* has an activating antidepressant effect, it should not be used in individuals with bipolar disorder who are vulnerable to becoming manic when given antidepressants or stimulants. Until this has been further studied, the authors advise caution in patients with bipolar spectrum disorders. The herb does not appear to interact with other medications, though it may have additive effects with other stimulants. It is best absorbed when taken on an empty stomach 30 minutes before breakfast and lunch. As with any herbal preparation, patients should inform their primary healthcare practitioner when taking *R. rosea*.

Rhodiola rosea One-year-old seedlings. Photo © 2002 Bertalan Galambosi

Figure 5: Salidroside



Rhodiola in the Future

More scientific research is needed to confirm the preventive and curative benefits of *R. rosea*. Controlled studies are warranted to explore its use in antidepressant augmentation, disorders of memory and cognition, attention deficit disorder, traumatic brain injury, Parkinson's disease, protection against arrhythmias, sports performance, aviation and space medicine (enhancing physical and mental performance while reducing stress reactions), endocrine disorders (infertility, premenstrual disorder, menopause), sexual dysfunction, disorders of the stress response system (fibromyalgia, chronic fatigue syndrome, and post traumatic stress disorder), and enhancement of chemotherapy/radiation with amelioration of toxicity.

In the course of evolution, *R. rosea* has adapted to the harsh conditions of high altitude (extreme cold, low oxygen, little rainfall, and intense irradiation from the sun) by producing a group of powerful protective compounds that have diverse beneficial effects in animals and humans. One is struck by the versatility of *R. rosea*, from its description in Greek medicine, 2000 years ago to its use by

20th century cosmonauts. It is time for modern research, using controlled clinical trials, to develop the potential medical applications of this unique phytoadaptogen.

Richard P. Brown, M.D., is Associate Clinical Professor of Psychiatry at Columbia University College of Physicians and Surgeons in New York City. He received his M.D. in 1977 from Columbia University College of Physicians and Surgeons in New York. Dr. Brown completed his Residency in Psychiatry and a Fellowship in Psychobiology and Psychopharmacology at New York Hospital. Dr. Brown is the recipient of numerous awards, including a Mead-Johnson Neuropsychopharmacology Travel Fellowship, a Mallinckrodt Scholar award, and a Fellowship in Neurosciences and Brain Imaging from the Dana Foundation. He has had a longstanding interest in herbal and complementary medicine, especially as relevant to psychiatry. In 2000, he co-authored the book, Stop Depression Now, *which presents a holistic approach to the treatment of depression, including SAM-e. Since 1999, Dr. Brown has taught a full day course on Herbs and Nutrients in Psychiatry at the annual meetings of the American Psychiatric Association. Dr. Brown has no financial interest in* Rhodiola rosea.

Patricia L. Gerbarg, M.D., is Assistant Clinical Professor in Psychiatry at New York Medical Center. She graduated from Harvard Medical School in 1975 and completed her Psychiatry Residency at Beth Israel Hospital in Boston in 1979. She finished psychoanalytic training at the Boston Psychoanalytic Society and Institute in 1992 and has maintained a private psychiatric practice for 23 years. Dr. Gerbarg has taught and lectured on a range of topics in psychiatry and psychoanalysis. Over the past eight years she has been increasingly involved in research and writing about alternative and complementary medicine in psychiatry and has co-authored numerous articles and book chapters with Dr. Brown. Dr. Gerbarg has no financial interest in Rhodiola rosea.

Roots of 5 year old cultivated ***Rhodiola rosea***. L. Mikkeli, Finland, 2002
Photo © 2002 Bertalan Galambosi

Zakir Ramazanov, Ph.D., D.S., is Professor of Biochemistry at Las Palmas Technological Institute, Spain. In 1978 he received a bachelor's degree with a double major in biochemistry and plant physiology from North Caucasian State University and in 1981 a Ph.D. in Plant Physiology and Biochemistry from the Soviet Academy of Sciences. He has served as Senior Scientist and Chief of the Department of Biotechnology at the Soviet Academy of Science and as Chairman of Algal Biotechnology Development. In 1991 he accepted a research fellowship at Louisiana State University. The recipient of numerous research grants, Dr. Ramazanov is known for his work in space biology, the cultivation of photosynthetic organisms in space stations, and the development of marine natural products from sea vegetables. He has published more than 140 scientific studies and co-authored two books: Arctic Root (Rhodiola rosea) — The powerful new Ginseng Alternative *(1998) and* Effective Natural Stress and Weight Management Using Rhodiola Rosea and Rhododendron Caucasicum *(1999). Dr. Ramazanov is President and CEO of National Biosciences Corporation, Chester, NY.*

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References

1. Engler A. *Syllabus der Pflanzenfamilien*. Vol. 2. Berlin, Germany: Borntraeger; 1964. p. 199-200.
2. Saratikov AS, Krasnov EA. *Rhodiola rosea is a valuable medicinal plant* (*Golden Root*). Tomsk, Russia: Tomsk State University Press; 1987.
3. Mell CD. Dyes, tannins, perfumes, and medicines from *Rhodiola rosea*. *Textile Colorist* 1938;60(715):483-4.
4. Linnaeus C. *Materia Medica*. Liber I. De Plantis. Stockholm, Sweden: Lars Salvius; 1749. p. 168.
5. Linnaeus C. *Örtabok*. Stockholm, Sweden: Almquist and Wiksell; 1725. p. 127.
6. Linnaeus C. *Plants of Lapland*. Uppsala, Sweden: The Royal Science Academy's documents; 1754. p. 182-7.
7. Linnaeus C. *Flora Oeconomica eller Hushålls-Nyttan af de i Swerige, Wildt wäxande Örter*. Stockholm, Sweden: Lars Salvii; 1748. p. 399.
8. Linnaeus C, Tonning H. *Norwegian Rarities*. Uppsala, Sweden: Johan Edman;1768. p. 3-19.
9. Sandberg F, Bohlin L. *Fytoterapi: växbaserade läkemedel* [*Remedies based on herbs*]. Stockholm, Sweden: Hälsokostrådets förlag AB; 1993. p. 131.
10. Commission Nationale de la Pharmacopée Française. *Pharmacopée Française*. IX ed. Table alphabétique revisée des drogues végétales. Paris, France: French Agence du Médicament–Direction des French Laboratoires et des Contrôles, Unité Pharmacopée; 1974. p. II A214-*101*.
11. Sandberg F. *Herbal Remedies and Herb Magic*. Stockholm, Sweden: Det Bästa; 1998. p. 223.
12. Mashkovskij MD. *Doctor's manual: medical drugs*. 12th ed. Vol. 1. Moscow, Russia: Meditzina; 1976. p. 161-5.
13. Khaidaev Z, Menshikova TA. *Medicinal Plants in Mongolian Medicine*. Ulan-Bator, Mongolia; 1978.
14. Magnusson B. *Fägringar: Växter som berör oss* (*Beauty: herbs that touch us*). Östersund, Sweden: Berndtssons; 1992. p. 66-7.
15. Hoppe H. *Drogen kunde*. Band 1, Angiosperm 8.Berlin, Germany: Walter de Gruyter; 1975. p. 986-7.
16. Nörr H. Phytochemical and pharmacological investigation of the adaptogens: *Eleutherococcus senticocus, Ocimum sanctum, Codonopsis pilosula, Rhodiola crenulata* [dissertation]. Munich, Germany: Faculty of Chemistry and Pharmacy, Ludwig-Maximilians-Universität München; 1993.
17. Krylov GV. *Herbs for Life*. Novosibirsk, Russia: Academic Press; 1969. p. 264.
18. Darbinyan V, Kteyan A, Panossian A, Gabrielian E, Wikman G, Wagner H. *Rhodiola rosea* in stress induced fatigue: a double blind cross-over study of a standardized extract SHR-5 with a repeated low-dose regimen on the mental performance of healthy physicians during night duty. *Phytomedicine* 2000;7(5):365-71.
19. Komarov VL, editor. *Flora of the USSR*. Volume IX, *Rosales* and *Sarraceniales*. Genus 698: *Rhodiola* L. Leningrad, Russia: The USSR Academy of Sciences: 1939. Translation: Jerusalem, Israel: Israel Program for Scientific Translation; 1971. p. 20-36.
20. Hegi G, editor. *Illustrierte Flora von Mitteleuropa*. Vol.IV/2, Liefering

2/3. Hamburg/Berlin, Germany; P. Posey: 1963. p. 99-102.
21. Ohba H. A revision of the eastern Himalayan species of the subgenus *Rhodiola* of the genus *Sedum*. In: Ohashi H, editor. *Flora of Eastern Himalaya*, 3rd report. Tokyo, Japan: University of Tokyo Press; 1975. p. 283-362.
22. Saratikov AS, Krasnov EA. Chapter I: Chemical composition of *Rhodiola rosea*. In: Saratikov AS, Krasnov EA. *Rhodiola rosea is a valuable medicinal plant* (*Golden Root*). Tomsk, Russia: Tomsk State University; 1987. p. 3-39.
23. Kurkin VA, Zapesochnaya GG. Chemical composition and pharmacological properties of *Rhodiola rosea*. *Chemical and Pharmaceutical Journal (Moscow)* 1986;20(10):1231-44.
24. Saratikov AS. *Golden Root (Rhodiola rosea)*. Tomsk, Russia: Tomsk State University Press; 1974.
25. Kurkin VA, Zapesochnaya GG. Chemical composition and pharmacological characteristics of *Rhodiola rosea* [review]. *Journal of Medicinal Plants, Russian Academy of Science, Moscow* 1985;1231-445.
26. Saratikov AS, Krasnov EA, Khnikina LA, Duvidson LM. Isolation and chemical analysis of individual biologically active constituents of *Rhodiola rosea*. Proceedings of the Siberian Academy of Sciences. *Biology* 1967;1:54-60.
27. The Russian Federation Ministry of Health and Medical Industry. *Russian National Pharmacopoeia*. Pharmacopoeia article: PA 42-2126-83, liquid extract of Rhodiola rosea root and rhizome. Moscow, Russia: The Russian Federation Ministry of Health and Medical Industry; 1983.
28. Dubichev AG, Kurkin BA, Zapesochnaya GG, Vornotzov ED. Study of *Rhodiola rosea* root chemical composition using HPLC. *Cemico-Parmaceutical Journal* 1991;2:188-93.
29. Ganzera M, Yayla Y, Khan IA. Analysis of the marker compounds of *Rhodiola rosea* L. (golden root) by reversed phase high performance liquid chromatography. *Chem Pharm Bull (Tokyo)* 2001;49(4):465-7.
30. Zhang S, Wang J, Zhang H. Chemical constituents of Tibetan medicinal herb *Rhodiola kirilowii* (Reg.). *Gansu Chung Kuo Chung Yao Tsa Chih* 1991;16(8):483, 512.
31. Wang S, Wang FP. Studies on the chemical components of *Rhodiola crenulata*. *Yao Hsueh Hsueh Pao* 1992;27(2):117-20.
32. Wang S, You XT, Wang FP. HPLC determination of salidroside in the roots of *Rhodiola* genus plants. *Yao Hsueh Hsueh Pao* 1992;27(11):849-52.
33. Bridel M, Beguin C. Isolation of rutoside, asparagines and a new glycoside, hydrolysable by emulsion, salidroside from *Salix triandra* L. *Séances Acad Sci* 1926;183:321-3.
34. Shi L, Ma Y, Cai Z. Quantitative determination of salidroside and specnuezhenide in the fruits of *Ligustrum lucidum* by high performance liquid chromatography. *Biomed Chromatogr* 1998;12(1):27-30.
35. Thieme H. On the identity of glucoside rhodioloside and salidroside. *Pharmazie* 1969;24(2):118-9.
36. Thieme H, Walewska E, Winkler HJ. Isolation of salidroside from leaves of *Rhododendron ponticum* x *catawbiense*. *Pharmazie* 1969;24(12):783.
37. The Russian Federation Ministry of Health and Medical Industry. *Russian National Pharmacopoeia*. Moscow, Russia: The Russian Federation Ministry of Health and Medical Industry; 1989.
38. Spasov AA, Wikman GK, Mandrikov VB, Mironova IA, Neumoin VV. A double-blind, placebo-controlled pilot study of the stimulating and adaptogenic effect of *Rhodiola rosea* SHR-5 extract on the fatigue of students caused by stress during an examination period with a repeated low-dose regimen. *Phytomedicine* 2000;7(2):85-9.
39. Spasov AA, Mandrikov VB, Mironova IA. The effect of the preparation rhodiosin on the psychophysiological and physical adaptation of students to an academic load. *Eksp Klin Farmakol* 2000;63(1):76-8.
40. Furmanowa M, Oledzka H, Michalska M, Sokolnicka I, Radomska D. Chapter XXIII *Rhodiola rosea* L. (Roseroot): *In vitro* regeneration and the biological activity of roots. Vol. 33. In: Bajaj YPS, editor. *Biotechnology in Agriculture and Forestry*. Vol. 33. *Medicinal and aromatic plants*. VIII. Berlin and Heidelberg, Germany: Springer-Verlag; 1995. p. 412-26.
41. Saratikov AS, Krasnov EA. Chapter VII: Adaptogenic properties of *Rhodiola rosea*. In: Saratikov AS, Krasnov, editors. *Rhodiola rosea is a valuable medicinal plant* (*Golden Root*). Tomsk, Russia: Tomsk State University Press; 1987. p. 194-215.
42. Petkov VD, Stancheva SL, Tocuschieva L, Petkov VV. Changes in brain biogenic monoamines induced by the nootropic drugs adafenoxate and meclofenoxate and by citicholine (experiments on rats). *Gen Pharmacol* 1990;21(1):71-5.
43. Baranov VB. Experimental trials of herbal adaptogen effect on the quality of operation activity, mental and professional work capacity. Contract 93-11-615 Stage 2 Phase I. Moscow, Russia: Russian Federation Ministry of Health Institute of Medical and Biological Problems; 1994.
44. Komar VV, Kit SM, Sischuk LV, Sischuk VM. Effect of *Rhodiola rosea* on the human mental activity. *Pharmaceutical J* 1981;36(4):62-4.

Rhodiola rosea. One year old seedlings transplanted into field covered with black plastic mulch. Mikkeli,Finland. Photo © 2002 Bertalan Galambosi

45. Stancheva SL, Mosharrof A. Effect of the extract of *Rhodiola rosea* L. on the content of the brain biogenic monoamines. *Medecine Physiologie Comptes Rendus de l'Académie Bulgare des Sciences* 1987;40(6):85-7.
46. Lazarova MB, Petkov VD, Markovska VL, Petkov VV, Mosharrof A. Effects of meclofenoxate and extr. *Rhodiolae rosea* L. on electroconvulsive shock-impaired learning and memory in rats. *Methods Find Exp Clin Pharmacol* 1986;8(9):547-52.
47. Petkov VD, Yonkov D, Mosharoff A, Kambourova T, Alova L, Petkov VV, et al. Effects of alcohol aqueous extract from *Rhodiola rosea* L. roots on learning and memory. *Acta Physiol Pharmacol Bulg* 1986;12(1):3-16.
48. Saratikov A, Marina TF, Fisanova LL. Effect of golden root extract on processes of serotonin synthesis in CNS. *Journal of Biological Sciences* 1978;6:142.
49. Marina TF, Alekseeva LP. Effect of *Rhodiola rosea* extract on electroencephalograms in rabbit. In. Saratikov AS, editor. *Stimulants of the Central Nervous System*. Tomsk, Russia: Tomsk State University Press; 1968. p. 22-6.
50. Marina TF. Effect of *Rhodiola rosea* extract on bioelectrical activity of the cerebral cortex isolated to a different extent from the brain. In. Saratikov AS, editor. *Stimulants of the Central Nervous System*. Tomsk, Russia: Tomsk State University Press; 1968. p. 27-31.
51. Brown RP, Gerbarg PG, Muskin PR. Alternative Therapies in Psychiatry. In: Tasman A, Lieberman J, Kay J, editors. *Psychiatry*. 2nd ed [in press]. West Sussex, England: Wiley & Sons, Ltd.; 2002.
52. Lupien SJ, de Leon M, de Santi S, Convit A, Tarshish C, Nair NP, et al. Cortisol levels during human aging predict hippocampal atrophy and memory deficits. *Nat Neurosci* 1998;1(1):69-73.
53. Furmanowa M, Skopinska-Rozewska E, Rogala E, Malgorzata H. *Rhodiola rosea* in vitro culture: phytochemical analysis and antioxidant action.

Acta Societis Botanicorum Poloniae 1998;76(1):69-73.
54. Durany N, Munch G, Michiel T, Riederer P. Investigations on oxidative stress and therapeutical implications in dementia. *Eur Arch Psychiatry Clin Neurosci* 1999;249 Suppl 3:68-73.
55. Joseph JA, Shukitt-Hale B, Denisova NA, Bielinski D, Martin A, McEwen JJ, et al. Reversals of age-related declines in neuronal signal transduction, cognitive, and motor behavioral deficits with blueberry, spinach, or strawberry dietary supplementation. *J Neurosci* 1999;19(18):8114-21.
56. Saratikov AS, Krasnov EA. Chapter VIII: Clinical studies of *Rhodiola*. In: Saratikov AS, Krasnov EA, editors. *Rhodiola rosea is a valuable medicinal plant* (*Golden Root*). Tomsk, Russia: Tomsk State University Press; 1987. p. 216-27.
57. Krasik ED, Morozova ES, Petrova KP, Ragulina GA, Shemetova LA, Shuvaev VP. Therapy of asthenic conditions: clinical perspectives of application of *Rhodiola rosea* extract (golden root). In. *Proceedings Modern problems in psycho-pharmacology.* Kemerovo-city, Russia: Siberian Branch of Russian Academy of Sciences: 1970. p. 298-330.
58. Krasik ED, Petrova KP, Rogulina GA, Shemetova LYa, Shuvayeva. New data on the therapy of asthenic conditions (clinical prospects for the use of *Rhodiola* extract). Proceedings of All-Russia Conference: Urgent Problems in Psychopharmacology 1970 May 26-29. Sverdlovsk, Russia: Sverdlovsk Press; 1970. p. 215-7.
59. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 4th ed (DSM-IV). Washington, DC: American Psychiatric Association; 1994.
60. Hickie I, Davenport T, Issakidis C, Andrews G. Neurasthenia: prevalence, disability, and healthcare characteristics in the Australian community. *Br J Psychiatry* 2002;181:56-61.
61. Merikangas K, Angst J. Neurasthenia in longitudinal cohort study of young adults. *Psychological Medicine* 1994;24(4):1013-24.
62. Lin TY. Neurasthenia revisited: its place in modern psychiatry. *Psychiatric Annals* 1992;22(4):173-87.
63. Zheng YP, Lin KM, Takeuchi D, Kurasaki KS, Wang Y, Cheung F. An epidemiological study of neurasthenia in Chinese-Americans in Los Angeles. *Comprehensive Psychiatry* 1997;38(5):249-59.
64. U.S. Department of Health and Human Services. *The International Classification of Diseases*. 10th Revision (ICD-10). Washington, DC: U.S. Department of Health and Human Services; 1992.
65. Zatova MI, Krilov GV, Saratikov AS. Golden root: new stimulative and adaptogenic drug. *Proceedings of Siberian Academy of Sciences. Biological and Medical Sciences*. 1965;2:111-9.
66. Saratikov AS. Screening for natural central nervous system stimulants. In: Saratikov AS, editor. *Stimulants of the Central Nervous System*. Vol. 1. Tomsk, Russia: Tomsk State University Press; 1966 p. 3-23.
67. Brichenko VS, Kupriyanova IE, Skorokhova TF. The use of herbal adaptogens with tricyclic antidepressants in patients with psychogenic depression. In: Saratikov AS, editor. *Modern Problems of Pharmacology and Search for New Medicines*. Tomsk, Russia: Tomsk State University Press; 1986. p. 58-60.
68. Mattson MP, Pedersen WA, Duan W, Culmsee C, Camandola S. Cellular and molecular mechanisms underlying perturbed energy metabolism and neuronal degeneration in Alzheimer's and Parkinson's diseases. *Ann N Y Acad Sci* 1999;893:154-75.
69. Saratikov AS, Krasnov EA. Chapter III: Stimulative properties of *Rhodiola rosea*. In: Saratikov AS, Krasnov EA, editors. *Rhodiola rosea is a valuable medicinal plant* (*Golden Root*). Tomsk, Russia: Tomsk State University; 1987. p. 69-90.
70. Panossian A, Wikman G, Wagner H. Plant adaptogens. III. Earlier and more recent aspects and concepts on their mode of action. *Phytomedicine* 1999;6(4):287-300.
71. Salnik BU. Effect of several stimulators on central nervous system energy metabolism during muscular workload [dissertation]. Tomsk, Russia: Tomsk State Medical Institute; 1970.
72. Adamchuk LB. Effects of *Rhodiola* on the process of energetic recovery of rat under intense muscular workload [dissertation]. Tomsk, Russia: Tomsk State Medical Institute; 1969.
73. Danbueva EA. Effect of stimulators of the central nervous system on lipid metabolism at different muscular workloads [dissertation]. Tomsk, Russia: Tomsk State Medical Institute; 1968.
74. Revina TA. Effect of stimulators of the central nervous system on carbohydrate and high energy phosphorylated compound metabolism in the brain during intense muscular workload [dissertation] Tomsk, Russia: Tomsk State Medical Institute; 1969.
75. Brekhman II, Dardymov IV. New substances of plant origin which increase non-specific resistance. *Ann Rev Pharmacol* 1968;(9):419-30.
76. Porsolt RD, Anton G, Blavet N, Jalfre M. Behavioral despair in rats: a new model sensitive to antidepressant treatments. *Eur J Pharmacol* 1978;47(4):379-91.
77. Borsini F, Meli A. Is the forced swimming test a suitable model for revealing antidepressant activity? *Psychopharmacology (Berl)* 1988;94(2):147-60.
78. Willner P. The validity of animal models of depression. *Psychopharmacology (Berl)* 1984;83(1):1-16.
79. Boon-Niermeijer EK, van den Berg A, Wikman G, Wiegant FA. Phyto-adaptogens protect against environmental stress-induced death of embryos from the freshwater snail *Lymnaea stagnalis*. *Phytomedicine* 2000;7(5):389-99.
80. Lishmanov IuB, Trifonova ZhV, Tsibin AN, Maslova LV, Dementeva LA. Plasma beta-endorphin and stress hormones in stress and adaptation. *Biull Eksp Biol Med* 1987;103(4):422-4.
81. Maslova LV, Kondratev BIu, Maslov LN, Lishmanov IuB. The cardioprotective and antiadrenergic activity of an extract of *Rhodiola rosea* in stress. *Eksp Klin Farmakol* 1994;57(6):61-3.
82. Gerasimova HD. Effect of *Rhodiola rosea* extract on ovarian functional activity. *Proc of Scientific Conference on Endocrinology and Gynecology*. Sverdlovsk, Russia. 1970 Sept 15-16. Siberian Branch of the Russian Academy of Sciences. p. 46-8. 83.Saratikov AS, Krasnov EA. Chapter VI: The influence of *Rhodiola* on endocrine glands and the liver. In: Saratikov AS, Krasnov EA, editors. *Rhodiola rosea is a valuable medicinal plant* (*Golden Root*). Tomsk, Russia: Tomsk State University; 1987. p. 180-93.
84. Maimeskulova LA, Maslov LN, Lishmanov IuB, Krasnov EA. The participation of the mu-, delta- and kappa-opioid receptors in the realization of the anti-arrhythmia effect of *Rhodiola rosea*. *Eksp Klin Farmakol* 1997;60(1):38-9.
85. Baranov VB. The response of cardiovascular system to dosed physical load under the effect of herbal adaptogen. Contract 93-11-615 Phase I and Phase II. Moscow: Russian Federation Ministry of Health Institute of Medical and Biological Problems; 1994.
86. Bolshakova IV, Lozovskaia EL, Sapezhinskii II. Antioxidant properties of a series of extracts from medicinal plants. *Biofizika* 1997;42(2):480-3.
87. Udintsev SN, Schakhov VP. Decrease of cyclophosphamide haematotoxicity by *Rhodiola rosea* root extract in mice with Ehrlich and Lewis transplantable tumors. *Eur J Cancer* 1991;27(9):1182.
88. Borovskaya TG, Fomina TI, Iaremenko KV. A decrease in the toxic action of rubomycin on the small intestine of mice with a transplantable tumor through the use of a Rhodiola extract. *Antiobiot Khimioter* 1988;33(8):615-7.
89. Udintsev SN, Krylova SG, Fomina TI. The enhancement of the efficacy of adriamycin by using hepatoprotectors of plant origin in metastases of Ehrlich's adenocarcinoma to the liver in mice. *Vopr Onkol* 1992;38(10):1217-22.
90. Udintsev SN, Shakhov VP. The role of humoral factors of regenerating liver in the development of experimental tumors and the effect of *Rhodiola rosea* extract on this process. *Neoplasma* 1991;38(3):323-31.
91. Salikhova RA, Aleksandrova IV, Mazurik VK, Mikhailov VF, Ushenkova LN, Poroshenko GG. Effect of *Rhodiola rosea* on the yield of mutation alterations and DNA repair in bone marrow cells. *Patol Fiziol Eksp Ter* 1997;(4):22-4.
92. Bocharova OA, Matveev BP, Baryshnikov AIu, Figurin KM, Serebriakova RV, Bodrova NB. The effect of a *Rhodiola rosea* extract on the incidence of recurrences of a superficial bladder cancer (experimental clinical research). *Urol Nefrol (Mosk)* 1995;(2):46-7.

Small Minority Accounts for Majority of Botanical Product Sales

According to a report in *Nutrition Business Journal*, Consumer Research in the Nutrition Industry II, consumers are expressing a strong and growing desire for better health through their beliefs, and, to a lesser extent, through purchases of food, supplements, and other healthy lifestyle products. Unfortunately, many consumers are also, at best, vague and, at worst, confused or ignorant about everything except basic nutritional messages.

Reviewing the results of *NBJ*'s annual consumer issue, it is clear that while researchers believe long-term trends for dietary supplements and organic, natural and functional foods remain positive, the industry relies upon a very "pliable" consumer. Consumers lack education in herbal science, brands, and regulations — without it they remain vulnerable to misconceptions and misinformation.

The information in the table below is compiled by *NBJ* from more than 30 credible consumer surveys and reconciled against manufacturer and retailer sales figures.

Perhaps most interesting, and most revealing, is not who is taking supplements, but who is *not*. *NBJ* concludes that about 45 percent of Americans don't take vitamins, 70 percent don't take herbal supplements, 75 percent don't take minerals, 85 percent don't take specialty supplements, and 95 percent don't take sports supplements. The numbers of rare and occasional users are also high, leaving a vast majority of sales in a small minority of the population for every category with the exception of multivitamins.

The full report, with data on all product categories, may be ordered by calling 619/295-7685 ext. 12, or online at <www.nutritionbusiness.com>.

—Karen Robin

Consumer Usage: Herbs & Botanicals 2000–2001

U.S Consumer Herbs/Botanicals Use 2000

Consumer Type	Population (mil.)	% of pop.	# of purchases /month	$ spent/ month	Annual Total ($mil.)	% of mkt.
Heavy Consumers	3.3	1.5%	2.5	$29.62	$1,178	29%
Regular Consumers	10.5	4.8%	1.0	$11.85	$1,492	36%
Occasional Consumers	17.7	8.0%	0.3	$3.47	$735	18%
Rare Users	33.7	15.3%	0.2	$1.78	$718	17%
Non-Users	155.7	70.5%	0.0	$0.00	—	0%
Totals	**221**		**Total Herbs/Botanicals**		**$4,123**	**100%**

U.S Consumer Herbs/Botanicals Use 2001

Consumer Type	Population (mil.)	% of pop.	# of purchases /month	$ spent/ month	Annual Total ($mil.)	% of mkt.
Heavy Consumers	3.3	1.5%	2.5	$29.47	$1,183	28%
Regular Consumers	10.6	4.8%	1.0	$11.79	$1,501	36%
Occasional Consumers	18.2	8.2%	0.3	$3.45	$752	18%
Rare Users	34.6	15.5%	0.2	$1.77	$733	18%
Non-Users	156.3	70.1%	0.0	$0.00	—	0%
Totals	**223**		**Total Herbs/Botanicals**		**$4,170**	**100%**

Source: *Nutrition Business Journal* (San Diego), derived from a variety of sources. Totals may not add up due to rounding.

Some figures are approximations that have been compiled from more than 20 consumer survey sources. These sources include The Hartman Group, Multi-Sponsor, Harris Interactive, The Natural Marketing Institute, Health Focus, Sloan Trends & Solutions, the U.S. Census Bureau, Food Marketing Institute, Q2 Brand Intelligence, Key Note, *Prevention Magazine*, Rodale, Roper ASW, Mintel International and SRI Business Intelligence. Usage figures vary greatly. The *Nutrition Business Journal* (NBJ) has made every effort to present accurate usage and buying patterns by reviewing all relevant sources of consumer data and reconciling this research against consumer expenditures estimated and published by NBJ. Although NBJ has made every effort to be accurate, all figures are not the result of direct surveys and therefore are not guaranteed to be accurate. Errors are unintentional.

Population figures assume 2000 pop=281m, 2000 adults=221m, 2001 pop=284m, 2001 adults=223m (m = million).

Farm Bill Bans Use of Name "Ginseng" on Non-*Panax* Species: "Siberian Ginseng" no longer allowed as commercial term

by Mark Blumenthal

The new Farm Security and Rural Investment Act of 2002 ("Farm Bill") has a provision that effectively bans the use of the name "Siberian Ginseng" and any other use of the term "ginseng" in a commercial herbal product unless it is used for an herb in the genus *Panax*. The new law, signed by President George W. Bush on May 13, 2002, makes the term "Siberian ginseng" for *Eleutherococcus senticosus* illegal in commerce on herb product labels, as well as in promotion literature and advertising.[1]

The term "Siberian Ginseng" has been used in the United States since *Eleutherococcus senticosus* (Rupr. & Maxim.) Maxim., Araliaceae was introduced as a commercial herbal product in the 1970s and since the publication of Richard Lucas' booklet *Eleuthero (Siberian Ginseng)*.[2] In the late 1970s there was considerable debate within the herb industry about the name. Ginseng purists did not want to see it sold with the common name ginseng as they did not consider it a true ginseng (i.e., in the genus *Panax*, which includes Asian ginseng, *P. ginseng*, and American ginseng, *P. quinquefolius*). Others with commercial interest in the importation of eleuthero argued, successfully at the time, that both genera are members of the family Araliaceae, both are used as adaptogens or tonics, and they are somewhat interchangeable in their use. The new Farm Bill now settles that old argument in favor of the purists, particularly those with an economic interest in the term "ginseng" here in the United States: ginseng farmers in Wisconsin.

A press release from the Ginseng Board of Wisconsin called for the immediate removal of "false products" from the U.S. market, stating, erroneously, that American and Asian ginseng are the "only two kinds of ginseng in the world."[3] Other species in commerce that qualify as ginseng include Japanese ginseng (*P. japonicus* C.A. Mey.) and Vietnamese ginseng (*P. vietnamensis* Ha & Grushv.).

The trend toward using the common name eleuthero for *E. senticosus* began as a movement within the herb industry itself, and was codified in the first edition of *Herbs of Commerce*.[4] In that 1992 publication, which lists approximately 550 herbs sold in the U.S. market, the name eleuthero was given as preferred over *Siberian ginseng* ("Other Common Name"). In 1997 the U.S. Food and Drug Administration (FDA) adopted *Herbs of Commerce* as an official list for common names of herb products sold in the United States. Subsequent federal regulations require that common names used on products be consistent with the names standardized in that edition of *Herbs of Commerce*.[5] Thus, eleuthero has been the preferred commercial name since 1997.

The second edition of *Herbs of Commerce*, published in 2000, also lists eleuthero as the "Standard Common Name;" Siberian ginseng is listed as an "Other Common Name" along with "Ussurian thorny pepperbush," a name proposed by Russian researchers that never received appreciable acceptance in commerce.[6]

The introduction to *Herbs of Commerce* states, "In no case is the listing of a common name in this ["Other Common Names"] field meant to imply that such a name is an acceptable option in identifying plants in labeling, and, in fact, only the Standardized Common Name is acceptable for this purpose."[6] The book's editors and AHPA officials anticipate that FDA will eventually adopt this second edition as its listing of standardized common names for herbs sold in the United States, but the FDA has not announced its acceptance.

The American Botanical Council reinforces this nomenclature in its publications. Eleuthero is the common name used in *HerbalGram* and the listings for *E. senticosus* in ABC's three books* have used this term.

Specific language

The Farm Bill provision contains the following language under Subtitle I — General Provisions:

Section 10806. Market Names for Catfish and Ginseng:

(b) Ginseng Labeling —

(1) IN GENERAL — Notwithstanding any other provision of law, for purposes of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 301 et seq.)

(A) the term "ginseng" may only be considered to be a common or usual name (or part thereof) for any herb or herbal ingredient derived from a plant classified within the genus Panax; and

(B) only labeling or advertising for herbs or herbal ingredients classified within that genus may include the term 'ginseng'.

(2) AMENDMENT — Section 403 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 343) (as amended by subsection (a)(2)) is amended by adding at the end the following):

'(u) If it purports to be or is represented as ginseng, unless it is an herb or herbal ingredient derived from a plant classified within the genus Panax'.

The ginseng provision was introduced into the Farm Bill by U.S. Sen. Russell Feingold (D-WI), presumably representing the interests of the fairly influential Wisconsin American ginseng growers lobby, including the Ginseng Board of Wisconsin, Inc. (GBW). According to a release from AHPA, the organization worked closely with Feingold's office "in developing this law in a manner that is consistent with current FDA regulations and AHPA's *Herbs of Commerce*. We were able to successfully show that their original approach, based on the chemistry of ginsenosides, was problematic. We were also persuasive in requesting that this legislation not attempt to amend DSHEA [the Dietary Supplement Health and Education Act of 1994]. Ultimately, however, it has been a principle cause of the Ginseng Board of Wisconsin to reserve the name 'ginseng' for plants of the genus *Panax*, and this legislation is the Ginseng Board's coup de grace on this issue."[7]

AHPA's reference to ginsenoside chemistry refers to the position taken by the Ginseng Board of Wisconsin, Inc. (GBW) that the chemistry of both *P. ginseng* and *P. quinquefolius* is characteristically different from the chemical structures in eleuthero. A GBW press release states that eleuthero "does not contain any ginsenosides (the [primary] active ingredients in ginseng) but contains Eleutherosides E and B. Some of

* ABC's three books are *The Complete German Commission E Monographs: Therapeutic Guide to Herbal Medicines* (1998), *Herbal Medicine: Expanded Commission E Monographs* (2000), and *The ABC Clinical Guide to Herbs* (in press).

the eleutherosides are glycosides, but they don't include the 'saponin glycosides that characterize Panax ginseng.'"[3]

On June 18, 2002, AHPA's President Michael McGuffin wrote to the FDA and the Federal Trade Commission (FTC), noting that AHPA nomenclatural policy was already codified as an industry standard by both editions of *Herbs of Commerce,* that the term ginseng was reserved for species in the genus *Panax*, and that eleuthero was already the standardized common name for *E. senticosus*.[7]

"AHPA fully understands and accepts the purpose and rationale of the Farm Bill's ginseng section and AHPA does not oppose this law," he wrote. However, McGuffin noted that many of AHPA's members need ample time to sell already manufactured products labeled Siberian ginseng, that some members still use the name Siberian ginseng, and he requested a moratorium to allow members to re-label future eleuthero products.

The AHPA letter requested the following:[7]

- Products labeled Siberian ginseng: a period of one year from May 13, 2002, within which to run out inventories of products containing eleuthero that are presently labeled as "Siberian ginseng."
- Products labeled eleuthero: a period of two years from May 13, 2002, within which to manufacture and ship products containing eleuthero that are labeled as eleuthero with parenthetical information that references the former name of "Siberian ginseng" (e.g., "formerly known as Siberian ginseng," or "formerly, Siberian ginseng").
- Advertising eleuthero: a period of two years from May 13, 2002, for manufacturers, distributors, and retailers to advise consumers in advertising that eleuthero was formerly known as "Siberian ginseng."

McGuffin stated that AHPA was in contact with Feingold's staff and the Wisconsin Ginseng Board of Trade on this matter and requested from FDA and FTC their agreement and assent to the AHPA proposal and a compliance timetable. As of the time of this writing (July 23), there was no word from either agency of their agreement to the proposal.

A report from the U.S. House Committee on Appropriations dated July 26, 2002, includes language introduced by U.S. Rep. David Obey (D-WI) that states an expectation that FDA will "take all appropriate action to expeditiously enforce" the new limits to the use of "ginseng" on product labeling or in advertising. Obey is the ranking minority member of the House Appropriations Committee, which includes the Subcommittee on Agriculture, Rural Development, Food and Drug Administration and Related Agencies.

AHPA reports that it has received a response to its requests from FTC, in which they stated, "While the FTC will coordinate with FDA and provide whatever assistance they may require in their enforcement of this new measure, we anticipate that FDA will take the primary role in implementing this amendment to their statute." The FDA had not yet responded.[8]

AHPA said they learned from Obey's office that the word "expeditiously" is not meant to instruct FDA to make this their most immediate priority, it is also clear that he will not support a full year of non-enforcement.

The U.S. Senate Agriculture Appropriations Subcommittee, chaired by Sen. Herb Kohl (D-WI), also has jurisdiction over the FDA budget, among other agencies. Like Obey, Kohl reportedly would like to see the law on this issue enforced expeditiously.

Although a relatively popular herb, eleuthero usually lags behind Asian ginseng in retail sales in most channels of trade and ahead of American ginseng. Market surveys are often unspecific about the type of ginseng being measured, so it is probable that such survey statistics can include sales for both American and Asian ginsengs as well as eleuthero. The AHPA letter cites a survey from *Nutrition Business Journal* stating that sales of "ginseng" were reported in 2000 to be $173 million, or 7.5 percent of all "single herbal category" sales.

The new legal provision also impacts the use of the word "ginseng" in relation to other species not in the genus *Panax* including so-called "Indian" or "Ayurvedic ginseng" for ashwagandha (*Withania somnifera* (L.) Dunal, Solanaceae), "Brazilian ginseng" for suma (*Hebanthe eriantha* (Poir.) Pederson, Amaranthaceae, syn. *Pfaffia paniculata* (Mart.) Kuntze, Amaranthaceae), and other terms that have exploited the term *ginseng* in commerce.

References

1. 107th Congress. Farm Security and Rural Investment Act of 2002. Public Law 107-171 <http:www.ers.usda.gov/Features/farmbill/>.
2. Lucas R. *Eleuthero (Siberian Ginseng): Health Herb of Russia*. R&M Books: Spokane (WA); 1973.
3. Ginseng Board of Wisconsin. Farm bill bans use of name "ginseng" on non-Panax species: Siberian ginseng, Indian ginseng, Brazilian ginseng, and others no longer allowed as commercial term (press release). Wausau, WI. 2002.
4. Foster S. *Herbs of Commerce*. Austin (TX): American Herbal Products Association; 1992.
5. 21 Code of Federal Regulations. Sec. 101.4(h)(1)-(2).
6. McGuffin M, Kartesz JT, Leung AY, Tucker AO. *Herbs of Commerce*. 2nd edition. Silver Spring (MD): American Herbal Products Association; 2000.
7. McGuffin M. Letter to JA Levitt, C Taylor, MK Engle, M Rusk. 2002, Jun 18.
8. Gellman R. Eleuthero/Ginseng. *AHPA Report*. 2002 September.

Samoan Village

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with a major article appearing in London's *Financial Times*. It is believe that the ARA-Samoa agreement is the first time that a pharmaceutical developer has agreed to return royalty shares on a drug to indigenous peoples and village healers.

"Ethnobotanical research in Samoa helped us to learn about this important natural resource and its potential for treating HIV," Barefield said. "It is only right that the people of Samoa share in any potential reward, and we hope that this agreement will set a standard on ethical dealings with medicines derived from indigenous cultures."

Cox, who originally discovered the plant, said that the signing of the agreement was one of the "happiest days" of his life. "As an ethnobotanist, my dream has always been to return some benefit to the indigenous people who have been so kind and caring to me over the years. I hope that the ARA-Samoa agreement will prove to be a useful model for benefit sharing in the future."

—Kim West

Reference:

1. Benefit sharing and prostratin [interview]. *Plant Talk*. 2002;27:38-9.
2. Kulkosky J, Culnan DM, Roman J, Dornadula G, Schnell M, Boyd MR, Pomerantz RJ. Prostratin: activation of latent HIV-1 expression suggests a potential inductive adjuvant therapy for HAART. *Blood* 2001 November 15;98(10):3006-15.

FDA Issues Final Rule Banning Use of Aloe and Cascara Sagrada in OTC Drug Products

by Holly J. Bayne, Esq.

On May 9, 2002, the U.S. Food and Drug Administration (FDA) issued a final rule banning the use of aloe (*Aloe* spp., Aloaceae) and cascara sagrada (*Frangula purshiana* (DC.) J.G. Cooper, Rhamnaceae; syn. *Rhamnus purshiana* DC.) as laxative ingredients in over-the-counter (OTC) drug products.[1] Under the new regulation, the botanical ingredients "aloe," "aloe extract," and "aloe flower extract," as well as "cascara sagrada" (including "casanthrol," "cascara fluid extract aromatic," "cascara sagrada bark," "cascara sagrada extract," and "cascara sagrada fluid extract") are deemed *not* "generally recognized as safe and effective" (GRASE) for use as stimulant laxative ingredients in OTC drug products. The regulation is scheduled to become effective on November 5, 2002. After that date, any OTC drug product containing aloe or cascara sagrada and labeled for laxative use that is introduced into interstate commerce will be considered a "new drug" in violation of federal law. No recall of products already on the market or in distribution has been suggested.

In response, on June 10, the American Herbal Products Association (AHPA) and the International Aloe Science Council (IASC) filed a joint petition with FDA ("AHPA/IASC Petition") requesting that FDA stay (i.e., set aside) the effective date of the regulation and reconsider the status of the aloe and cascara sagrada ingredients.[2] The AHPA/IASC Petition challenges FDA's final rule on both legal and scientific grounds, arguing that aloe and cascara sagrada ingredients cannot be deemed to be "new drugs" because they are GRASE based on readily available information. Although FDA regulations require the FDA Commissioner to "promptly review" such petitions, there is no time frame imposed upon the Commissioner to act.[3]

Overview of FDA's OTC Drug Review

The ban is part of FDA's OTC Drug Review, an ongoing administrative review process begun in 1972 to determine which active ingredients are GRASE for use in OTC drug products. Drugs that are generally recognized by qualified experts as safe and effective for their labeled uses are not subject to FDA premarket approval requirements applicable to "new drugs."[4] Generally, only active ingredients used in OTC drug products in the United States prior to December 1975 were included in the Review. To facilitate the process, FDA divided OTC drugs into therapeutic classes and set up advisory panels to consider safety, effectiveness, and labeling (i.e., indications, warnings, and directions for use). In general, each panel prepared a report that was published by FDA in the *Federal Register* for public comment as an advance notice of proposed rulemaking. The reports set forth the conditions (i.e., active ingredients, therapeutic claims, and labeling) under which the panels believed the products are GRASE and not misbranded. This classification is known as "Category I." The panels also identified the conditions under which they believed OTC drugs are *not* GRASE (that is, "Category II"), or not classifiable because there were insufficient data at the time of the review to make a decision regarding safety or efficacy ("Category III").

Under the OTC Drug Review procedures, after consideration of comments to a panel report, FDA publishes a "tentative final monograph" (TFM), which has the legal status of a "proposed rule." After considering comments to the TFM, FDA issues a final monograph (final rule), which is eventually codified in the Code of Federal Regulations (CFR). OTC drugs that comply with the specifications of a final monograph are not "new drugs" and may be marketed without FDA approval of a new drug application.

FDA's review of laxative drug products

In 1975, FDA's Advisory Review Panel on OTC Laxative, Antidiarrheal, Emetic, and Antiemetic Drug Products recommended that aloe and cascara sagrada ingredients be classified GRASE for laxative drug use.[5] In January 1985, FDA published a proposed rule (TFM) setting forth the conditions under which OTC laxative drug products are GRASE and not misbranded.[6] In that TFM, the stimulant laxative ingredients "aloe" and "cascara sagrada ingredients" are classified as GRASE, that is, "Category I," for use in OTC drug products when labeled in accordance with the TFM, which mandates certain warning statements.

The 1985 TFM also classified "sennosides A and B" derived from certain senna (*Senna alexandrina* Mill., Fabaceae; syn. *Cassia senna* L.) sources (fruits and leaves) as GRASE for stimulant laxative OTC drug use.

In 1998, FDA proposed amending the TFM to reclassify aloe, cascara sagrada, and senna ingredients from GRASE ("Category I") to "Category III" (i.e., more data needed).[7] FDA issued the proposed rulemaking apparently after considering data and information on the safety of bisacodyl, senna, and "two related" anthraquinone laxative ingredients, danthron and phenolphthalein. Formerly, phenolphthalein was the active ingredient in leading over-the-counter laxatives marketed by the pharmaceutical industry.[8]

The proposed reclassification was based on FDA's conclusion that aloe, cascara sagrada, and senna contain anthraquinone ingredients which require mutagenicity, genotoxicity and carcinogenicity tests to confirm safety. In a notice of proposed rulemaking published in the *Federal Register* on June 19, 1998, FDA indicated that the Center for Drug Evaluation and Research (CDER) Carcinogenicity Assessment Committee (CAC) "has recommended that the anthraquinone laxatives (aloe, cascara sagrada, and senna) and bisacodyl be tested in the standard battery of genotoxicity tests and under the test conditions by which phenolphthalein was found to be positive."[9] At that time, FDA advised interested persons to consult with the agency concerning carcinogenicity testing requirements and protocols before initiating such testing. FDA also indicated that, if data were not provided or were deemed to be inadequate for aloe, cascara sagrada, and senna (and bisacodyl), the ingredients would be deemed not GRASE and placed in "Category II."[10] In response, FDA received safety data only on senna (and bisacodyl) and has indicated that these ingredients will be addressed in a future issue of the *Federal Register*.

In issuing the May 2002 ban on the use of aloe and cascara sagrada in OTC laxative drugs, FDA concluded that, because inter-

ested persons (e.g., members of the pharmaceutical and dietary supplement industries) failed to submit new data from carcinogenicity studies for these ingredients, they are not GRASE. Thus aloe and cascara sagrada ingredients will not be included in the forthcoming final monograph for OTC laxative drugs. The FDA has determined that these ingredients should be eliminated from laxative drug products within 180 days of publication of the final rule (i.e., November 5, 2002), regardless of whether toxicology testing is undertaken in the future.[11] While companies are encouraged to comply with the regulation immediately, products containing aloe and cascara sagrada may be marketed and distributed through November 4. Beginning November 5, existing inventory on market shelves may continue to be sold until it is gone, but no further distribution will be permitted.

The AHPA/IASCS petition

The AHPA/IASC Petition seeks a stay in the effective date of the regulation until FDA and a relevant Advisory Committee have reconsidered the action. Principally, the Petition argues that:

- the failure of interested persons to submit testing data requested by FDA does not invalidate the general recognition of safety and effectiveness of aloe and cascara sagrada confirmed by the Advisory Committee that initially reviewed the data;
- FDA does not have the statutory authority to unilaterally decide the requirements of general recognition of safety and efficacy; and
- aloe and cascara sagrada meet the legal standard for "general recognition of safety" established by FDA's own regulations which state: "a low incidence of adverse reactions or significant side effects under adequate directions for use and warnings against unsafe use … proof [of safety] shall include results of significant human experience during marketing … ."[12]

AHPA and IASC also assert that FDA failed to consider relevant data and readily available information and conclusions of qualified experts, including information contained in AHPA's *Botanical Safety Handbook*, published in 1997.[13] In addition, FDA apparently failed to consider relevant work by other notable expert bodies. The German Commission E lists both aloe and cascara sagrada as approved botanical drug ingredients for use in the treatment of constipation, according to certain use restrictions.[14] Consumers are advised to obtain laxative effects through the use of bulk forming laxatives prior to use of aloe or cascara sagrada. The World Health Organization (WHO) also recognizes clinical data on aloe for the short-term treatment of occasional constipation,[15] as do the monographs published by the European Scientific Cooperative on Phytotherapy (ESCOP).[16]

The Petition also cites an American Botanical Council publication, *Herbal Medicine: Expanded Commission E Monographs,* noting its review of evidence regarding cascara sagrada, the first Western use of which was reported by an Eclectic physician in 1877.[17]

The AHPA/IASC Petition also challenges FDA's rule under the Regulatory Flexibility Act, which requires an agency to consider regulatory options to minimize the economic impact of rulemaking on small businesses, *if* a rule will significantly impact a substantial number of them. The FDA, in both the 1998 proposed rule and final regulation banning aloe and cascara sagrada ingredients, determined this rulemaking would not have a significant economic impact on a substantial number of small entities. In its Petition, AHPA/IASC argue that FDA's determination is flawed because the agency did not consider the effects of the final rule on companies that manufacture and market dietary supplements containing aloe and cascara sagrada as laxative ingredients, as well as the effects on companies selling aloe as a food or dietary supplement product for non-laxative use. Previously, FDA has recognized that most of the manufacturers and distributors of dietary supplements meet the definition of a "small business." [15]

Future actions

Currently, it is uncertain whether FDA will act on the AHPA/IASC Petition in a timely manner. However, FDA is not likely to revise the regulation to permit the use of aloe and cascara sagrada in OTC laxative drugs unless industry submits new data. Industry could submit to FDA new toxicological testing data or data concerning general recognition of safety as part of a citizen petition to amend the monograph. Under FDA procedures, the agency must act on such petition within 180 days.

Alternatively, new data concerning aloe or cascara sagrada could be submitted to FDA as part of a new drug application (NDA) to obtain prescription or OTC marketing status. This route appears highly unlikely due to the huge investment in time and money that such undertaking would require, particularly since these ingredients are not patentable. Moreover, although an "innovator" company can generally expect five years of marketing exclusivity for a drug approved by FDA under a NDA (regardless of any patent protec-

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FDA Ban

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tion), this may not provide enough of a financial incentive to pursue the NDA route.

The final rule could have a far-reaching impact on the status of dietary supplements containing aloe and cascara sagrada that are sold for laxative effects, and possibly on other products that have not been proven safe by toxicological testing procedures despite long-term use. FDA fails to address these issues in its ruling. As a matter of law, it may be argued that FDA's final rule banning the use of aloe and cascara sagrada in OTC laxative drug products would not cover dietary supplements containing these ingredients. Still, it would appear that FDA's classification of aloe and cascara sagrada ingredients as *not* generally recognized as safe for OTC drug laxative use could form a basis for the agency to attempt to assert that the ingredients are not safe for dietary supplement or other food use.

Indeed, FDA has recognized an overlap between OTC drug claims and permissible structure-function claims for dietary supplements. In FDA's final rule concerning the permissible scope of structure-function claims for dietary supplements (implementing a provision of the Dietary Supplement Health and Education Act of 1994), FDA indicates that certain laxative-type claims may be made in dietary supplement labeling. A dietary supplement may include labeling claims indicating the product is intended to relieve "occasional constipation," which can arise from a variety of causes unrelated to disease.[16]

Importantly, FDA also indicates that a dietary supplement containing an ingredient covered by an OTC drug monograph, and bearing claims in labeling covered by the monograph, may be misbranded (that is, illegal) if material information required under the monograph is omitted from the labeling of the dietary supplement. In the final analysis, FDA's new regulation clearly implicates the status of aloe and cascara sagrada supplements sold for their laxative effects, and possibly other food and dietary supplement products. This is an issue that demands the attention of the dietary supplement industry, and, as the AHPA/IASC Petition argues, must be addressed by FDA.

Holly J. Bayne is an attorney based in Washington, D.C. at the Law Office of Holly Bayne, P.C., who specializes in advising companies on regulatory and business issues concerning food, dietary supplement, and botanical products.

Reference:

1. 67 *Federal Register* 31125 (May 9, 2002).
2. Docket No. 78-N-036L, American Herbal Products Association and the International Aloe Science Council, Petition for Reconsideration and Petition for Stay of Action, Status of Aloe Ingredients and Cascara Sagrada Ingredients as Over-the-Counter Drug Active Ingredients ("AHPA/IASC Petition"). 2002 June 10.
3. 21 Code of Federal Regulations. Sections 10.33, 10.35.
4. 21 Code of Federal Regulations. Sections 321(p), 355.
5. 40 *Federal Register* 12902 (March 21, 1975).
6. 50 *Federal Register* 2124 (January 15, 1985).
7. 63 *Federal Register* 33592 (June 19, 1998).
8. FDA reopened the administrative record on danthron and phenolphthalein in the *Federal Register* of September 2, 1997 (62 *Federal Register* 46223), and discussed carcinogenic risk of these ingredients. When

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FTC Commissioner Wants More Rigorous Self-Regulation in Dietary Supplement Industry

by Mark Blumenthal

Federal Trade Commissioner Sheila F. Anthony has called on members of the dietary supplement industry to implement additional and improved self-regulation and said that the media should refuse to run supplement ads that contain claims that are obviously false.

Adding that she was speaking for herself (her term is to expire September 2002) and not for other commissioners or the Commission as a whole, Ms. Anthony told an audience at the Food and Drug Law Institute's 45th Annual Educational Conference in Washington, D.C. in April that, since passage of the Dietary Supplement Health and Education Act (DSHEA), there has been a "dramatic increase in the marketing of supplements and, with that increase, we have seen more examples of questionable claims ... ."

Anthony named two factors that have had a significant influence over this growth. The first is the Internet, which has made it easier for unscrupulous marketers to sell their products globally. The second is the erroneous belief among some supplement marketers that DSHEA provides a green light to make implied health and disease claims and thus avoid FDA review or approval, which is clearly not the case. Consequently, the FTC has brought over 60 enforcement actions in the past five years challenging false or unsubstantiated claims about the efficacy and safety of a wide variety of dietary supplements, "and we have many more in the pipeline," she said.

"We are also looking broadly at the question of who has liability for deceptive advertising claims," she said. Guidelines published by the FTC in 1998 stated, "...all parties who participate directly or indirectly in the marketing of dietary supplements have an obligation to make sure that claims are presented truthfully and to check the adequacy of the support behind these claims."

Anthony noted that the FTC has acted against manufacturers and marketers, their ad agencies, and expert or celebrity endorsers of products in ads. "Many egregious claims — particularly for weight loss products — often appear in the mainstream media. Major national newspapers, magazines, television, cable, and radio stations seem ready to accept the substantial advertising dollars of this industry without question, often airing patently fraudulent ads with claims of extreme, instant and effortless weight loss ... . While many publications screen ads for taste and appropriateness, they appear reluctant to take a few extra steps to weed out obvious fraud," she said.

She said that more measures should be taken to protect the American public against false, deceptive or misleading ads. "The Commission uses a variety of means to combat deceptive claims for dietary supplements. But more needs to be done. I believe that there needs to be more and better self-regulation in the dietary supplement industry. The industry must step up to the plate and take a more active role in policing those in their industry who are engaged in fraud and deception, and are giving the entire industry a black eye," she noted, suggesting that there are responsible and ethical companies whose image is tarnished by those who would mislead the consumer.

"I also believe that the media has an exceptionally important role to play through media screening of problematic ads," Anthony said. "I hope that the media also steps up to the plate and chooses to forgo placing ads that result in a fraud on the public, who, after all, are their customers too."

[Anthony SF. Combating Deception in Dietary Supplement Advertising [Remarks before the Food and Drug Law Institute 45th Annual Educational Conference, Washington, DC]. 2002 April 16. Available online <http://www.ftc.gov/speeches/anthony/dssp2.htm>]

FDA

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FDA announced that it planned to ban phenolphthaleins, Novartis reformulated Ex-Lax® to include sennosides as the active ingredient in its regular and maximum strength formulas. In a similar fashion, Schering-Plough reformulated Correctol®. Bayer dropped Phillips' Gelcaps®.

9. 63 *Federal Register* 33592 (June 19, 1998).
10. Common herbal ingredients such as, "prune powder," "prune concentrate dehydrate," Chinese rhubarb (*Rheum palmatum* L., and *R. officinale* Baill., Polygonaceae) and frangula or buckthorn (*Frangula alnus* Mill., Rhamnaceae; syn. *Rhamnus frangula* L.) are included among the list of "Category II" stimulant laxative ingredients. FDA did not determine these laxative ingredients are unsafe and/or ineffective, nor has it done so with respect to aloe and cascara sagrada. Rather, there were insufficient data in the administrative record to confirm safety and/or efficacy. These ingredients *defaulted* to "Category II" status according to FDA procedures. Both Chinese rhubarb and frangula are popular stimulant laxatives in Europe, approved by the German Commission E.
11. 67 *Federal Register* 31126 (May 9, 2002)
12. AHPA/IASC Petition at 3-5. See also 21 Code of Federal Regulations. Section 330.10(a)(4)(i).
13. AHPA/IASC Petition at 5-7. See also McGuffin M, Hobbs C, Upton R, Goldberg A, editors. *American Herbal Products Association's Botanical Safety Handbook*. Boca Raton (FL): CRC Press LLC; 1997. p. 7-8, 96, 177-9, 183.
14. Blumenthal M, Busse WR, Goldberg A, Gruenwald J, Hall T, Riggins CW, Rister RS, editors. Klein S, Rister RS, translators. *The Complete German Commission E Monographs: Therapeutic Guide to Herbal Medicines*. Austin (TX): American Botanical Council; Boston (MA): Integrative Medicine Communication; 1998. p. 80-1, 104-5.
15. World Health Organization. *WHO monographs on selected medicinal plants*. Vol. 1 Geneva, Switzerland: World Health Organization; 1999. p. 33-48. Note: WHO differentiates aloe ("the dried juice of the leaves of *Aloe vera* ... or *A. ferox* ... and its hybrids... ." used for treatment of constipation) from aloe vera gel ("the colourless mucilaginous gel obtained from the parenchymatous cells in the fresh leaves of *Aloe vera*" traditionally used for external treatment of minor wounds and skin irritations).
16. European Scientific Cooperative on Phytotherapy. *Monographs on the medicinal uses of plant drugs*. Fascicule 5. Exeter, United Kingdom: ESCOP; 1997.
17. AHPA/IASC Petition at 6. See also Blumenthal M, Goldberg A, Brinckmann J, editors. *Herbal Medicine: Expanded Commission E Monographs*. Newton (MA): Integrative Medicine Communications; 2000.
18. AHPA/IASC Petition at 9-14. See also 60 *Federal Register* 67211 (Dec. 28, 1995).
19. 65 *Federal Register* 1000, 1015 (Jan. 6, 2000).

Industry Takes the Lead in the Conservation of U.S. Botanicals

by David Hircock, B.Pharm., MRPS, MNIMH

The medicinal and aromatic plant industries have a tradition of sharing new research, exploring product development, and clarifying consumer safety issues. However, the perspective of First Peoples usually was not included, nor were conservation data. Adding both to the agenda made the *Industrial Leadership for the Preservation of Medicinal and Aromatic Plants* a unique experience for participants. The symposium brought all stakeholders into the discussion and provided a forum for the exchange of multidisciplinary information.

A two-day symposium held February 26 and 27, 2002, *Industrial Leadership for the Preservation of Medicinal and Aromatic Plants*, brought together Native American elders, conservationists, botanists, scientists, industry members, and government officials to address their shared growing concerns for the future conservation of domestic North American wild botanical resources, as well as the status of foreign botanicals used in the United States. Facilitated by the Plant Conservation Alliance–Medicinal Plant Working Group (PCA-MPWG), a consortium of federal agencies and non-federal cooperators working collectively for native medicinal plant conservation, the symposium was sponsored by industry leaders such as Aveda, American Herbal Products Association, the Steven Foster Group, Inc., GlaxoSmithKline, and the American Botanical Council. The symposium was held in Philadelphia's Sheraton Rittenhouse Hotel, a leading "green" hotel in the United States that combines quality lodging with environmentally responsible business principles such as energy conservation and the use of recycled materials.

U.S. Fish and Wildlife Service Assistant Director Kenneth Stansell (left) presents the agency's 2002 Corporate Wildlife Stewardship Award to Dominique Conseil, president of Aveda, at the Industrial Leadership symposium. © 2002 Aveda.

With the setting of the Rittenhouse as a daily reminder of the environmental difference committed leadership can make, symposium speakers described some of the steps taken to ensure the sustainability of various plant species: for example, Aveda's work on sandalwood (*Santalum album* L., Santalaceae), Strategic Sourcing's work with goldenseal (*Hydrastis canadensis* L., Ranunculaceae), and Glaxo SmithKlein on black cohosh (*Actaea racemosa* L., Ranunculaceae, syn. *Cimicifuga racemosa* (L.) Nutt.). Distinguished researchers, industry leaders, and First Peoples shared new ways to help balance conservation, business, and cultural concerns associated with medicinal and aromatic plant use.

Gary Paul Nabhan, Ph.D., Director of the Center for Sustainable Environments at Northern Arizona University, and the symposium keynote speaker, summed up the importance of the two days, saying, "Overcoming differences that distanced us from one another in the past, representatives from many cultures, professions and regions found common ground on how to *conserve and use* native medicinal plants."

To honor the source of our earliest native plant knowledge and to emphasize that respectful plant use also requires respectful relationships with native peoples, the symposium began with a traditional blessing, led by Canoncito Navajo Spiritual Elder Leon Secatero, who was assisted by other PCA-MPWG Elders' Circle members from six tribes based in the United States. The Elders' Circle is a committee of representatives from the Navajo, Mohawk, Yurok, Catabwa, Cherokee, Kumeyaay, and Accohanock tribes, invited by members of the MPWG to take a strong leadership role in native medicinal plant conservation.

The blessing established the tone and direction for the two days of presentations and discussions. It also signalled the critical role these elders played, both in endorsing the symposium and in guiding program development. "The elders say you must take care of the land and your surroundings to fulfill your sacred path and become part of Mother Earth's beautiful gift," Secatero said in explaining the commitment of native peoples to exploring cooperative efforts with industry and other organizations to help reverse the loss of biodiversity.

As a symposium sponsor, Dominique Conseil, President of Aveda, also expressed why the symposium was important to him as a businessman, "At Aveda, we think there is no responsible alternative to doing business in an environmentally sustainable way. We see the challenge of environmental sustainability as one of protecting biodiversity. Caring for endangered species starts in our own backyard, with the aromatic and medicinal plants we use as an industry."

A Sampling of Presentations

Speakers came from as far away as India and as close as Pennsylvania to share a message of joint cooperation for the benefit of medicinal and aromatic plants.

Akash Chopra, Ph.D., CEO of Biosys Group, Rothamsted, UK, shared examples of successful projects that demonstrate the benefits of traceability (tracking a product back to where its raw materials originated), including eliminating adverse effects on the environment and communities at the same time that they establish a fair price structure and eliminate the causes of product adulteration. Transparency, according to Chopra, allows all stakeholders in the supply chain to engage from a position of mutual understanding, makes all stakeholders responsible for the overall issues, and builds trust as well as the ability to incorporate values into the system that benefit all partners. Chopra ended his presentation with a simple statement: "On behalf of Mother Earth and those who cannot be here to speak for themselves, we have shown that we have a collective responsibility, as stakeholders, in the use and preservation of natural resources, and there should be a fair distribution of the commercial proceeds."

Bruce Stein, Vice President of NatureServe, Rosslyn, Virginia, provided an environmental context with which to begin to evaluate the sustainable use of native U.S. plants. According to Stein, the

United States has approximately 16,000 native vascular plants — about 7 percent of the world's total — 4,000 of which are found nowhere else. The United States does share many plants at the level of family and genus with Asia, including American ginseng (*Panax quinquefolius* L., Araliaceae) and mayapple (*Podophyllum peltatum* L., Berberidaceae). NatureServe assesses the status of many plants, based on selected criteria: number of populations, abundance of range, trends, threats, intrinsic fragility. The NatureServe database <www.natureserve.org/explorer> provides a source of authoritative conservation information on more than 50,000 plants, animals and ecosystems in the United States and Canada. Stein concluded by offering several recommendations: 1) improve monitoring of both trade volumes and field population conditions; 2) monitor data that are comparable across sites and species; 3) look at broader impacts on ecosystems; and 4) engage the professional botanical community and mobilize volunteers.

Native American elders Tismal Crow (left) and Leon Secatero blessed the symposium with a traditional invocation. © 2002 Aveda.

Michael McGuffin, president of the American Herbal Products Association (AHPA), defined issues of sustainability for the global marketplace, with particular emphasis on U.S. native species. Based on knowledge of the trade in these species, he offered tools that could be considered to help ensure sustainability: proper harvesting practices; industry consumption data; cultivation; substitutes; national and international regulations; and botanical data. He ended on a hopeful note, citing a remark made in 1903 by Henry Kraemer, editor of the *American Journal of Pharmacy* and the preeminent pharmacognosist of his day: "We believe that Americans will be as successful in the conservation of their forests and wild plants and animals as they have been original, fearless and fortunate in the discovery of her treasures and the development of her resources."

Trish Flaster, President and CEO of Botanical Liaisons of Boulder, Colorado, addressed quality control in a context different from how it is usually presented. In her words, quality control spans the entire process — from soil to soul, from seed to consumer. Documentation of the process at each stage is critical because the chain of custody of plant material is huge given the size of the market. Also, if quality control does not include native knowledge, even support for native languages, which are being lost at alarming rates, then knowledge of the plants is diminished as is biodiversity. Flaster emphasized the importance of talking to the people in the field, "They have a knowledge base of how to collect, when to collect, where to collect. Do not separate the people and the plants. With the respect for the people you then have the respect for the Earth, and when we can keep respect for the Earth and its many gifts, then we are able to pass them forward to the generations to come."

Leon Secatero, Spiritual Leader of the Canoncito Navajo of New Mexico and Tis Mal Crow, Hitichiti Cherokee elder from Tennessee, spoke extensively on the Native American perspective concerning the state of American wild herbs. "In my language," said Tis Mal Crow, "we have 45 words for snow, 65 words for rain, but no words for extinct. It is a foreign word. But now this word has an impact on me. When I was young I thought there would be no end to the plants I worked with, but now I know that this word is a real thing."

Ann Koontz, Director of EnterpriseWorks, of Washington D.C., discussed balancing environmental, social, and business issues in the aromatic plants and essential oils arena. She stressed the need to balance a variety of factors: 1) the growing demand for aromatic products worldwide; 2) the fact that the people closest to the resource are often poor, with few resources to manage sustainable harvesting; 3) absence of knowledge concerning sustainable yields and harvesting practices for many species; and 4) the continued loss of many aromatic plants found in biodiversity-rich areas due to over-harvesting and other threats. Koontz provided examples from Nepal of successfully balancing these factors by: 1) looking at all the players, their functions, and technologies and their role in a sector's markets, paired with threat analysis to understand the range of resource degradation; 2) using economic benefits as the entry point to working with producers while balancing environmental and social equity issues; and 3) promoting linkages with multiple players to increase producer benefits.

Uwe Koetter, Ph.D., Director of New Products Research for GlaxoSmithKline Consumer Healthcare in Parsippany, New Jersey, introduced his company's work with G. Harnischfeger, Schaper & Brummer, in the cultivation of black cohosh. GlaxoSmithKline contracts for cultivation to achieve improved quality and consistency of plants. Its goals also include sustainability, purity, and reliability.

David Hircock, herbalist consultant to Aveda based in New York, New York, used sandalwood as an example of Aveda's commitment to sustainability. Hircock posed the question: "How do we investigate sustainability, and what happens when we find a potential problem?" In the case of sandalwood, Aveda sourced its raw materials from India, until it began to suspect sandalwood was being poached. Knowing how old a sandalwood tree must be to produce oil, the company began to require suppliers to submit documents proving that Indian sandalwood oil was supplied from legal Indian government sources. When suppliers failed to demonstrate progress, Aveda took steps to ensure a sustainable and traceable supply of the oil. Research suggested that poachers who illegally cut down sandalwood trees also poached Asian elephants as another

source of income and were involved in various human rights violations. Rather than continuing to source materials from the wild, Aveda sought alternatives. As an interim measure, it used sandalwood from Australia, because that country has strict laws of sustainability controlled by the Sandalwood Act and Wildlife Conservation Act, among other legislation. However, Aveda also seeks to continue to support sandalwood in India by purchasing from plantations and forest collectors with reliable traceability and sustainability programs.

Other speakers included: Steven Foster, noted American native plant expert; Peggy Olwell, PCA chair; Julie Lyke, former PCA-MPWG chair; Ed Fletcher, cultivation manager for Strategic Sourcing, Inc.; Danna J. Leaman, Ph.D., IUCN Medicinal Plant Specialist Group chair; Charlotte Gyllenhaal, University of Chicago; Tensie Whelan, Rainforest Alliance Executive Director; Monique Simmonds, Royal Botanical Gardens, Kew, England; Barry Dimson, President and CEO of Sheraton Rittenhouse Square; Michelle Penna, Director for Business Development for EcoEnterprises Fund; Bruce Mannheim, attorney with Bennett, Turner & Coleman; Kelly McConnell, NatureServe; Diane Don Carlos, United Plant Savers; Jennifer Morris, Manager of Enterprise Development and Support at Conservation International; Pierre Franchomme, Aromatic Sourcing; and Freddie Ann Hoffman, Pfizer, Inc.

Results

Industrial Leadership in the Preservation of Medicinal and Aromatic Plants was a remarkable event in which people who seldom have the occasion to interact found that they share the same goals. At the end of the symposium, approximately 125 people representing more than 60 organizations reached consensus on the following:

1. We endorse the Plant Conservation Alliance (PCA), and the Plant Conservation Alliance-Medicinal Plants Working Group (PCA-MPWG) and its Mission.
2. We acknowledge that we are all stakeholders in the preservation of plants.
3. We recognize that we need guidance from our indigenous elders.
4. We intend to develop a more formal structure for industry participation in PCA and PCA-MPWG.
5. We will hold another Industrial Leadership meeting in about one year to assess our progress toward formalizing a structure.

In addition, the group agreed to move forward with an Industry Committee, chaired by AHPA's Michael McGuffin. The committee seeks participants to help carry out its agenda. Further, the following action were identified:

1. Native American spokespeople continuing to send the message that the plants are sacred.
2. video distribution of this event to interested herb schools and other organizations.
3. existing standards for sustainable harvest promided to the MPWG (Partners: Rainforest Alliance and Center for Sustainable Environments).
4. survey of tonnage of wild medicinal plants produced/harvested in 2001 (Partners: AHPA, USFWS).
5. CITES (the Convention on International Trade in Endangered Species of Wild Fauna and Flora) implementation for native medicinal plants (Partners: AHPA, USFWS).

The goal now is to follow up on the intention to meet again next year. By 2003, the second meeting of *Industrial Leadership in the Preservation of Medicinal and Aromatic Plants* will report on progress to advance knowledge of the sustainability of these important plants.

David Hircock is an environmental watchdog and herbalist for the Aveda cosmetics company. British born, he holds degrees in pharmacy and herbal medicine.

Expo Asia in Hong Kong, May 15-17, 2002

by Alicia Goldberg

Expo Asia, sponsored by New Hope Natural Media during May 2002, was the first natural products trade show in Asia. It was surprisingly active, with 200 exhibitors representing 25 countries, and 4,000 buyers from 50 countries. The mix of buyers included 35 percent retailers, 18 percent suppliers, and 11percent manufacturers.

Hong Kong is the place to do business, serving as the English-speaking gateway to China and the rest of Asia. The tradeshow floor buzzed with genuine excitement and eagerness to do business. Big deals happened easily, with time for in-depth conversations. The New Hope team was friendly and well-organized, utilizing a staff of local experts that successfully secured media coverage in both English and Chinese papers.

Filled with light and perched on the bay, the Hong Kong convention center may be the most beautiful in the world. Some attendees took a moment to watch small traditional boats sail past large cruise ships, while sipping oolong tea. The conference layout was difficult to navigate, despite the small size, however, New Hope provided areas with tables and chairs that were useful to conduct meetings.

The main American companies with booths were NOW Foods, Jarrow, and Capsugel, taking advantage of a window of opportunity without competition. Several American companies sent representatives without setting up booths. Elephant Pharmacy, a start-up retail chain integrating a conventional pharmacy with natural remedies, sought innovative products backed by quality control and clinical research. Other American companies, such as the Ayurvedic product line Ayurceutics, chose to use the U.S. Commerce booth to distribute information.

The companies that exhibited from China were typically large manufacturers with university affiliations, with facilities based on Good Manufacturing Practices and clinical studies. However, most labeling was not U.S.-compliant, and they were not yet selling to the U.S. marketplace. Other countries represented included Australia, New Zealand, and the Philippines, with a booth focused on new cosmetic soaps, beauty masks, and bath powders.

New Hope regarded the show as the most successful first show it had ever produced. Executive producer Andrew Work enthusiastically restated New Hope's commitment to Expo Asia as key to the future expansion of the natural products industry.

Alicia Goldberg is director of Phytomed International, based in Austin, Texas. Her email address is <phytomedaustin@hotmail.com>.

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* This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Monroe E. Wall 1916–2002

Monroe E. Wall, Ph.D., a renowned natural products chemist whose discoveries defined the utility of botanical sources for cancer therapeutics, died of heart and kidney failure on July 6, 2002 in Chapel Hill, North Carolina. Dr. Wall was just three weeks shy of his 86th birthday at the time of his death. A dedicated and passionate investigator — who for more than 40 years was a commanding presence in the Research Triangle Park, NC, scientific community — Dr. Wall had worked continuously with his laboratory group at Research Triangle Institute (RTI) until just two weeks before his death.

Dr. Wall and Mansukh C. Wani, Ph.D., his colleague for more than 35 years, are credited as co-discoverers of the anticancer drugs paclitaxel, from the Pacific yew tree (*Taxus brevifolia* Nutt., Taxaceae), and camptothecin, from *xi shu* or "happy tree" (*Camptotheca acuminata* Decne., Cornaceae), a native Chinese tree that had been introduced to the United States. These discoveries were among hundreds of natural compounds identified by Dr. Wall and Dr. Wani.

Paclitaxel and camptothecin particularly stand out because each agent reveals previously unknown ways of killing cancer cells, and emphasizes the utility of plants as a source of drugs. In this post-genomic period of biology, where scientists are faced with thousands of potential drug targets that seek small molecule ligands, the contribution of paclitaxel and camptothecin to identify novel anticancer strategies cannot be understated. In the last century, only two other pairs of discoveries are of the same magnitude: the discovery of histamine H_2 antagonists and β_1-adrenoceptor antagonists, which earned Sir James W. Black, the 1988 Nobel Prize in Medicine, and the discovery of adrenergic and cholinergic agonists, which earned the 1936 Nobel Prize in Medicine for Sir Henry Hallett Dale and Otto Loewi.

Paclitaxel and camptothecin share interesting, yet distinct, stories. Originally isolated and characterized in 1971, the anticancer mechanism of action of paclitaxel was not evident until 1979 when a young New York scientist, Susan Band Horwitz, Ph.D., asked for a sample of the new drug. Now president of a leading cancer research society, the American Association for Cancer Research, the then-junior Dr. Horwitz demonstrated that paclitaxel uniquely promoted the overpolymerization of microtubules within cancer cells, effectively inhibiting cell division. Paclitaxel is now known as Taxol®, the original generic name coined by Wall and Wani, which was selected by Bristol-Myers Squibb as the trade name of this anticancer drug.

J. Paul Eder, M.D., clinical director of the experimental therapeutics program at the Dana-Farber Cancer Institute, calls the discovery of paclitaxel, "One of the most significant clinical advances in cancer therapy in the last decade. Paclitaxel has increased the cure rate of metastatic ovarian cancer, breast cancer, and has important activity in lung cancer. It is essential to note that it took nearly 25 years from the time of Dr. Wall's initial discovery until the first clinical trials of paclitaxel began, underscoring the difficulties in bringing new agents to the clinic."

In contrast, camptothecin was initially unsuccessful as an anticancer drug due to severe toxic reactions during human trials sponsored by the National Cancer Institute (NCI) in the early 1970s. However, camptothecin has led to two semisynthetic derivatives, topotecan (Hycamtin®, manufactured by GlaxoSmithKline, Philadelphia) and irinotecan (CPT-11; Camptosar®, by Pharmacia & Upjohn Company, Peapack, New Jersey) as well as a number of other camptothecins currently in clinical development.

The development of camptothecins is an outstanding example of the partnership between folk medicine and modern synthetic chemistry because the naturally occurring molecule would have failed as a drug if not for the intervention of medicinal chemistry. In fact, the discovery of camptothecin (1966) preceded that of paclitaxel (1971). A. Robert Jeffcoat, Ph.D., RTI director of bioorganic chemistry research, credits Dr. Wall's perseverance in the realization of camptothecins as therapeutic agents.

"Without Dr. Wall's persistence," Dr. Jeffcoat said, "camptothecin would likely have been discarded by NCI, and the discovery of the mode of action by which it prevents cancer growth would have been significantly delayed."

It was not until 1985 that the laboratory of Leroy F. Liu, Ph.D., who was then at Johns Hopkins University, demonstrated conclusively that camptothecin acted to create an unusual type of DNA damage in cancer cells by trapping the enzyme topoisomerase I during its normal action in regulating DNA structure.

Monroe Wall was born on July 25, 1916 and grew up in Newark, New Jersey, earning his bachelor's, master's, and doctoral degrees from Rutgers University. His early work focused on the nutritional requirements of the tomato plant, the crop most responsible for New Jersey's designation as The Garden State. In 1941, Dr. Wall married his wife, Marian, and joined the U.S. Department of Agriculture (USDA) in Philadelphia where he researched agricultural sources for products essential to the war effort, such as alternatives to rubber. During the 1950s most of his research focused on the search for phytosteroids that could serve as precursors for cortisone. In doing so, he collected thousands of plant extracts. A serendipitous 1957 visit to USDA by NCI pioneer, Jonathan Hartwell, M.D., changed Wall's focus in a way that would chart the next 40 years of his efforts.

Hartwell had been a student of folk medicine and recognized that nature might also provide treatments for cancer. Dr. Hartwell seized upon the late 19th century folk use of the mayapple (*Podophyllum peltatum* L., Berberidaceae) by the Penobscot Indians of Maine for cancer. The same plant was also used by physicians in Louisiana and Mississippi for venereal warts. One of its components, podophyllotoxin, was later demonstrated to have anticancer activity in mice. In his role at the Cancer Chemotherapy National Service Center, Hartwell convinced Wall to send him 1,000 ethanolic plant extracts for antitumor activity testing. More than a year later, word came back that one possessed particularly potent activity: an extract from *Camptotheca acuminata*.

Since anticancer drug discovery was not a focus of the USDA, Wall's drive to identify this plant's anticancer component was tempered until July 1960, when he was recruited to establish a chemistry program and

Robert "Bob" L. Saso 1943–2002

The Santa Cruz, California community of herbalists lost a dear friend on January 21st of this year. Bob Saso, herb gardener extraordinaire, passed away at the young age of 58 after fighting colon cancer for several years. Bob stayed close to home with his community herb work and so his name may not be familiar to the herbalist community at large. However, many are likely to be familiar with Bob's parents, Virginia and Louie Saso of Saso Herb Garden fame, formerly of Saratoga, California. The senior Sasos have touched many lives within the herbalist community, sharing their boundless wisdom and love for the cultivation of medicinal plants. Saso Herb Garden has been an icon in the growing medicinal herb movement for decades, educating many apprentice students and hosting herbal medicine classes for more than 25 years.

Bob followed in the footsteps of his parents on a parcel of land in the beautiful Santa Cruz Mountains, teaching people how to grow medicinals, teaching others about the beauty of plants, and otherwise simply loving the land. For more than 20 years Bob cultivated herb gardens in Felton, California where he welcomed people to share in his botanical bounty. Bob's enthusiasm to teach the community about herb cultivation led him to start a nursery and the Sierra Pacific school. He was also an avid softball player. His coed team of family and friends, the Blue Jays, won a championship in his honor in November. He is survived by his wife Susan, and their seven children and stepchildren.

Services for Bob were held on February 2 at St. John's Catholic Church in Felton. The church was filled to overflowing with friends and family members, attesting to the number of people who loved and respected him. Memories of Bob's enthusiasm, great smile, and beautiful gardens continue to inspire all those who had the honor of knowing him.

Contributions in Bob's name may be made to the Hospice Caring Project of Santa Cruz, 6851 Soquel Drive, Aptos, CA 95003.

— Darren Huckle
herbalist
Roy Upton
Executive Director, American Herbal Pharmacopoeia

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natural products group at the newly created Research Triangle Institute. From this beginning, RTI has become an internationally recognized research park, employing more than 40,000 in government, pharmaceutical, chemical, and computing research organizations. Wall recruited to RTI a number of young scientists, including Wani, many of whom went on to their own distinguished scientific careers. C. Edgar Cook, Ph.D., who worked with Wall and Wani on camptothecin and later directed the RTI Chemistry and Life Sciences unit that Dr. Wall founded, fondly describes the "Monroe Doctrine" as the basis of Wall's success: "Get good people, support them with good facilities, do good science, work hard, and keep doing it."

Another Wall recruit who also headed the same unit, F. Ivy Carroll, Ph.D., remarked, "Dr. Wall was much more than a scientist who conducted natural products research. His colleagues here at RTI and scientists all over the world have been inspired by his keen managerial ability combined with his people skills and warm concern for others."

Certainly, Dr. Wall's scientific accolades and hard-nosed, no-nonsense exterior belied the warm heart within. Jane Righter, his administrative assistant for the last 12 years of his career, recalled, "He gave regularly to charities and I have seen him offer loans to postdoctoral fellows when they first arrived at RTI, helping them before they received their first paycheck."

Susan Mayton, another close administrative colleague, remarked, "To the world, Dr. Wall was a brilliant scientist, but to those of us who were privileged to see him on a personal level, he was a warm and caring gentleman. That a man of his stature would have time to express sympathy over the loss of my mother or concern over my grandson's leukemia touched my heart deeply."

In fact, as Drs. Wall and Wani received the 2000 Charles F. Kettering Prize for Cancer Research, the highest honor in the field of cancer research, Wall remarked that the knowledge that his discoveries saved or improved the quality of life of, literally, millions of people was far more satisfying than any award or prize.

This past summer, Dr. Wall's contributions continued to be recognized. Over a year in development, RTI announced plans in July to carry on his legacy by creating the Wall and Wani Fellowships in Natural Products Research. These fellowships will to enable young scientists from around the world to train with Dr. Wall's group, now led by Dr. Wani and Nicholas H. Oberlies, Ph.D. (see http://www.rti.org/wallwani).

In August, with Wani and Oberlies in attendance, representatives from the U.S. Forest Service, the USDA, and the American Society of Pharmacognosy (ASP) held a plaque dedication ceremony in Washington state near the site of the original 1962 collection of *Taxus brevifolia* for the NCI screening program. ASP also held the 3rd annual Monroe E. Wall Symposium as part of its 2002 annual research meeting, which was conducted, appropriately, at Wall's alma mater, Rutgers University.

John M. Pezzuto, Ph.D., dean of Purdue University Schools of Pharmacy, Nursing, and Health Sciences reflected many shared sentiments in stating, "Having been affiliated with Monroe over the last 15 years has been one of the greatest honors of my life. Everyone recognizes him as a major icon of natural product drug discovery, but relatively few have had the privilege of knowing his incredible wit, sense of humor, and single-minded devotion toward beating the cancer problem. His passing is a great loss to society and the scientific community; I miss him greatly."

—David J. Kroll, Ph.D.
Senior Research Pharmacologist
Natural Products Laboratory
Center for Organic and Medicinal Chemistry
Research Triangle Institute
with contributions from Dr. Oberlies and Dr. Wani

Other tributes to Dr. Wall may be found online at <www.rti.org> and the July 11, 2002 issue of The New York Times. The website of the American Society of Pharmacognosy <www.phcog.org> includes links to both.

Biodiversity and Traditional Knowledge: Equitable Partnerships in Practice. edited by Sarah A. Laird. Earthscan Publications Ltd., London; Sterling, Virginia, <www.earthscan.co.uk>. 2002, paperback, v-xxxviii + 504 pp. ISBN 1-85383-698-2 (not available through ABC).

The Commercial Use of Biodiversity: Access to Genetic Resources and Benefit-Sharing. by Kerry ten Kate and Sarah A. Laird. Earthscan Publications Ltd., London, UK, <www.earthscan.co.uk>. 1999, v-xvii + 398 pp., hardcover. ISBN 1-85383-334-7 (not available through ABC).

These two books represent the state-of-the-art knowledge on the links between plants, people, cultures, products, profits, and ethics. Any company, scientist, herbalist, consumer, lawyer, government official, or curious person who wishes to learn how to work with local communities, traditional knowledge, and government agencies will find that these books provide information, case studies, and a wealth of detailed information. In fact, when the Convention on Biological Diversity (CBD) marks its 10-year anniversary in Johannesburg, South Africa (called Rio + 10) this September, these books should be provided to every official delegate.

These books will be of increasing importance to any and all companies that create new plant-based products as well as to ethically minded consumers who use botanical medicines, dietary supplements, and many plant-based health and beauty aids. They could also serve as core texts for a wide variety of high school and college-level courses on phytomedicines, globalization, ethics, product development, anthropology, ethnobotany, and international law.

Just recently published, *Biodiversity and Traditional Knowledge* is a spectacular contribution from the People and Plants Conservation Series, a collaboration of the World Wildlife Fund (WWF), the Kew Royal Botanic Gardens, and the United Nations Educational, Scientific and Cultural Organization (UNESCO). This edited volume contains 21 case studies from 16 countries. The case studies examine fascinating relationships in such diverse countries as Fiji, Norway, South Africa, Costa Rica, Cameroon, Uganda, Panama, and many others.

The authors and contributors, all 75 of them, are leaders in their fields of expertise. They bring a broad range of backgrounds to this complex topic, including law, ethnobotany, conservation and environmental sciences, and the perspective of local communities. This book also provides an invaluable directory of useful contacts and resources, including national government access and benefit-sharing contacts in Brazil, Ecuador, India, Costa Rica, Fiji, and eight other countries. It lists the websites of inter-governmental organizations, selected NGOs, research institutes, and organizations that work on biodiversity research and prospecting issues, as well as contact information for indigenous people's organizations in many parts of the planet.

The second book, *The Commercial Use of Biodiversity*, is the perfect companion volume to *Biodiversity and Traditional Knowledge*, and a very readable and engaging overview of access to genetic resources and benefit-sharing. Sections that focus on the botanical medicine industry, natural products for research, natural personal care and cosmetic industry, and horticulture will likely be of great interest to *HerbalGram* readers.

This book also provides numerous fascinating case studies. One of the most interesting and germane to natural products companies focuses on the marketing of a "public domain" plant species, annatto (*Bixa orellana* L., Bixaceae), a well-known source of red dye from the Amazon basin. The case study describes the relationship created by the Aveda Corporation with the indigenous Yawanana people in Brazil, detailing the entire process that Aveda has undertaken to work with these people, beginning in 1993. It is highly instructive to see the step-by-step evolution of such a project undertaken by a socially responsible company.

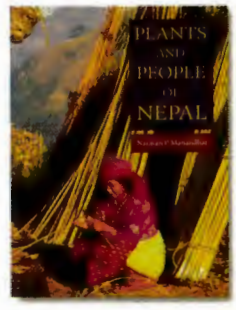
Another case study that I found of great interest discusses the development of a benefit-sharing partnership in Vietnam that focuses on a "new" species of Vietnamese ginseng (*Panax vietnamensis* Ha & Grushv., Araliaceae), which was not yet in international commerce.

Both of these books illuminate the how, who, where, and why of creating and maintaining equitable partnerships with local communities, national governments, and regional scientists while developing new products for a variety of marketplaces. These books build an excellent foundation in the fast-changing world of international ethics and benefit sharing. The next time you read a label, or hear a person or a company describe the ethical and socially responsible way that they have created a new product by working with the wisdom of indigenous cultures, you will be able to differentiate the short-term hustler from the more committed company or person.

Both of these books clearly show the links between the conservation of ecosystems, the needs of local communities, and the influence of the market economy. In this age of demonized globalization and events like 9/11, we all need to strive to create a more equitable, sharing, and collaborative business environment. My thanks to these authors for shining the light on how to do so in our complex and ever-changing multicultural universe.

—Steven R. King, Ph.D.
Senior Vice President of Ethnobotany and Conservation, Shaman Botanicals.com

Plants and People of Nepal, by Narayan P. Manandhar. 2002. 636 pp, illustrated hardcover. ISBN 0-88192-527-6. $69.95. ABC Catalog # B519.



When Timber Press puts its imprimatur on an ethnobotany book, the title typically establishes a new standard of excellence in its category. Thus, when Narayan Manandhar's *Plants and People of Nepal* came off the press, my expectations were high. Still, I was caught off guard by the breadth of what is offered in this book. Like Daniel Moerman's *Native American Ethnobotany*, also published by Timber Press in 2000, *Plants and People of Nepal* is not only a vast body of work, but is

a career summary of a prolific scholar and researcher. Dr. Manandhar has handed us the keys to the botanical treasury of the Kingdom of Nepal, from its most remote and inaccessible corners to the well-trammeled Kathmandu Valley.

Dr. Manandhar is no stranger to academic rigor. Educated first at universities in Kathmandu, Nepal, and Bihar, India, he earned his doctorate in economic botany at the Scientific and Medical University of Grenoble, France. Upon his return to Nepal, he worked in that country's national herbarium. He applied himself to the systematic survey of Nepal's people and plants, a body of work that spanned 30 years. Then he set about to write *Plants and People of Nepal*.

Dividing the 600-page book into four large chapters, Dr. Manandhar establishes first a geographic foundation for the reader, describing the geography, climate, vegetation zones, and conservation concerns of Nepal. He maps and identifies all 75 districts in the country, every single one of which he has visited. Early on, the author emerges not only as an astute scholar, but as a seasoned and understated explorer as well. While others have investigated Asia in large expeditions (á la Roy Chapman Andrews of the New York Museum of Natural History, whose Central Asia Expeditions in the 1930s electrified world imagination), Manandhar has investigated the full length and breadth of Nepal, including a number of extremely remote and difficult areas, largely alone and on foot.

Moving into a discussion of the people of Nepal, Dr. Manandhar reveals a broad diversity of ethnic backgrounds and languages. A major crossroads of Asia, the Kingdom of Nepal is home to 60 or so ethnic communities, mostly divided into two major groups, Indo-Nepali and Tibeto-Nepali. Like native American or Amazonian tribes, these various peoples have evolved unique customary uses of native plants, which represent a vast agricultural and ethnomedical variety.

Plants and People of Nepal offers a full 36 pages of color photographs, all of which show the daily uses of various plants among Nepalese people. The photography is well done, and the number of pictures is quite generous, but I still wanted more, to enjoy a further glimpse of fascinating peoples in remote places with their medicinal plants, yeast cakes, spices, fruits, grains, baskets, and traps. But this is not a complaint born of any deficiency in the book; it just made me want more.

In his elucidation of the ethnobotany of Nepal, Dr. Manandhar describes that country's history of plant use, agriculture, medicinal and fiber plants, and flora employed for yet other purposes such as dyes, decorations, and fish poisons. That material, plus the preceding information, sets the stage for the stunning centerpiece chapter of the book, The Useful Plants of Nepal, which, along with two related appendices, occupies nearly 500 of the remaining pages. Here, the reader is treated to a sprawling library, a feast for the botanical intellect. The author provides everything you might expect, including Latin binomial and local names of plants, morphological descriptions, and medicinal and other uses. Finely executed line drawings by the author make the plant section of the book delightful to browse, and give visual depth to descriptions of the plants themselves. Clearly, he has worked and re-worked each plant description.

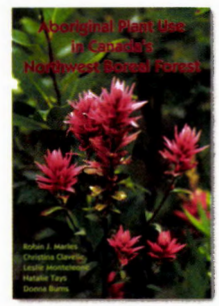
If the plant descriptions in this book are missing anything at all, it is more detailed information on their preparation. I would have enjoyed more insight into specific methods by which various medicinal species especially are juiced, mashed, ground, and made into infusions or poultices. But I would not say that this absence leaves the book lacking. Rather, it sets the stage for a variety of future herbal compendia that can delve more deeply into the specifics of that country's botanical pharmacopeia.

It's a tricky business to adequately summarize a book like this, especially considering that it represents the brilliant and apparently tireless career of a world-class scholar. That said, *Plants and People of Nepal* emerges as a bedrock volume, a collector's piece to be sure, but one which every collector should open and read and browse again and again. While India has produced a plethora of excellent ethnobotanical guides, Nepal has remained comparatively elusive until now. Thanks to decades of travel, study, and fastidious data collection, Narayan Manandhar has produced the definitive work on the ethnobotany of the Kingdom of Nepal. In doing so, he has established a place at the apogee of that region's botanical knowledge, and has given other researchers a worthy resource that will serve the interests of botanical scholarship and ethnomedical research for a long time to come. Bravo!

— Chris Kilham
Author, ethnobotany lecturer
University of Massachusetts

Aboriginal Plant Use in Canada's Northwest Boreal Forest, by Robin J. Marles, Christina Clavelle, Leslie Monteleone, Natalie Tays, Donna Burns. Published by University of British Columbia Press and Natural Resources Canada, Canadian Forest Service, distributed in the U.S. by University of Washington Press, 2000. 368 pp., color illustrations, hardcover. ISBN 0-7748-0737-7. $75.00; softcover ISBN 0-7748-0738-5 $24.95.

The significance of *Aboriginal Plant Use in Canada's Northwest Boreal Forest* lies not just in its content and scope, but perhaps moreso in what it represents as a participatory research partnership.



Although ethnobotany has gained global prominence over the past few decades, studies focused on the plant use of indigenous peoples of North America are relatively few, for a couple of reasons. Firstly, a view of some standing holds that most information about food, medicine, and other aspects of aboriginal culture has already been recorded, or is too eroded by Euroamerican acculturation to merit further scholarly attention. More recently, considerations of intellectual property and other aspects of indigenous rights have redefined the modes and paradigms through which ethnobotany is conducted. Canada, where relationships between First Nations communities and the larger society remain politicized over issues of title and sovereignty, might seem particularly unlikely ground for original research, particularly that touching on the contentious issue of medicinal plants. This volume admirably dispels both of these assertions.

To their credit, the authors, led by Robin Marles, built a preparatory research project during several years of progressive collaboration among university scientists, governmental resource and environment agencies, and First Nations communities. In a nonpolemic manner, they simply got on with the job and produced a volume that should be valued by and acceptable to most parties. In this case the level of education and political sophistication of aboriginal people in Canada becomes more an asset than an impediment for scientific research as it sets the groundwork for more equitable relationships and research agreements.

Members of indigenous communities actively involved themselves in the project as students, interviewers, community leaders, contributors of information and co-authors, and in the first instance, the resultant volume will serve as a resource most useful to the communities. Not only does it provide a wealth of information given by elders, but it places this information within the context of previously published ethnobotanical literature and a broad range of pharmacological, botanical, economic, ecological, and other scientific data. Communities can draw on this body of information to manage and use their own resources for subsistence, and social and economic benefit. In representing the wealth of traditional culture, this book offers a potential source of pride and continuity to peoples facing complex problems adjusting to ongoing lifestyle changes. I would hope also that it inspires additional aboriginal youth who wish both to embrace their own culture and to seek education and career opportunities in the sciences.

The main body of the volume comprises a series of more than 200 short monographs on the economic plants of the boreal forest in an area defined principally by the northern half of Manitoba, Saskatchewan, and Alberta and adjacent areas in the Northwest Territories and Nunavut, and representing the cultural heritage of Cree, Dene and Métis peoples. Data complied from original and secondary sources are combined under the categories of vernacular and scientific names; habitat; medicinal, technological, and ritual uses; properties including nutrient, toxic, and pharmacological constituents. Detailed botanical descriptions compliment high-quality color photographs; all information is well-supported by references to original field data or published literature and a practical glossary and index. Each entry finishes with an evaluation of the potential of the plant for economic development.

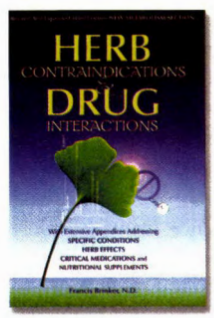
With its high level of scholarship and its practical orientation, this volume will also interest non-aboriginal scientists, entrepreneurs, and resource managers. Certainly, it supports the objective of sustainable use and management of the boreal forest, a priority for the Canadian Forest Service and other government agencies that funded the project.

Commercialization, whether by aboriginals or others, presents a dilemma for many First Nations in that it simultaneously offers a means to self-sufficiency on their own land while threatening traditional values and relationships with this environment. In this book, the evaluation of a few of the plants as offering appreciable commercial potential dispels this issue to a degree. Moreover, information that was deemed confidential for spiritual or proprietary reasons, including many details of the use of medicinal plants, has been withheld. In fact, much of the information contained is available in published sources. While the consultative model embraced by the project goes a long way to allay concerns within aboriginal communities, the end result is undoubtedly a compromise. Among the contending considerations of indigenous rights, economic needs and sustainable resource management, this volume strikes a successful balance between the traditional generosity of First Nations people to share with others and the necessity to serve the best interests of their own communities.

—Timothy Johns, Ph.D.,
Professor, School of Dietetics and Human Nutrition;
Centre for Indigenous People's Nutrition and the Environment, McGill University

Herb Contraindications & Drug Interactions, 3rd Edition. by Francis Brinker, N.D. 2001. 432 pp., softcover. ISBN 1-888483-11-3. $25.95. ABC Catalog #B282.

An increasingly common question asked of healthcare providers is, "Will this herbal product interact with the other medication that I am taking?" This book compiles the voluminous amount of scientific information, making it extremely useful when answering questions concerning herbal safety.



The first two editions of *Herb Contraindications & Drug Interactions* have been widely used for basic information on herb-drug interactions and contraindications. This third edition updates and adds to the information found in the earlier editions, and continues to be an outstanding resource for healthcare providers, especially pharmacists and physicians. In addition, the book will assist consumers who self-administer herbal medicines. Continuing a feature that began in the first edition, the author uses common diagnostic terms, rather than scientific and medical terminology, to foster lay readers' understanding (e.g., high blood pressure instead of hypertension). He also highlights many of these terms to call attention to specific health concerns, such as pregnancy, prolonged use, or children.

Several important changes have been made to this edition. To begin, the main section of the text, which is devoted to herbal contraindications and drug interactions, has expanded to 249 herbals. Second, common herb names have been standardized to the names designated in the second edition of the American Herbal Products Association's *Herbs of Commerce*. This should reduce confusion when searching for information in the book. Third, drug interactions have been categorized into four categories based on levels of evidence, including: (I) information obtained from human or pharmacological studies, case reports, or clinical experience; (II) data obtained from animal research; (III) speculative data based on in vitro studies or evaluations based on known mechanisms of action; and (IV) dubious information based on flawed or uncertain evidence. In addition, the appendices have been expanded and include 614 herbs and 17 vitamins/minerals as to their affect on organ systems, certain conditions and in combination with specific drugs. Lastly, several new appendices have been added to the book.

The book is divided into six sections: an introductory section, the main section of the book, an appendixes section, a brief addendum (Complementary Interactions of Herbs with Drugs), the cited references, and the easy-to-use index that cross-references the entire text. The introduction includes a forward on the need for information on herb-drug information and contraindication written by Colin Nicholls, editor of the *British Journal of Phytotherapy*. The preface and introduction provide an overview and introduction on how to use the book.

The main section of the book provides a wealth of authoritative information on herbal contraindications and drug interactions. The entries are presented alphabetically (from *Acacia* to *Yohimbe*) by common plant name, followed by the scientific binomial and a listing of common names used in other countries or by Native Americans. Each contraindication and drug interaction is documented as to the category of evi-

dence and the reference sources are cited within the text. Reference sources include primary literature and authoritative secondary resources. In addition, English-language abstracts were used occasionally.

The second half of the book includes four comprehensive referenced appendices: Appendix A, herbs to be used with caution; Appendix B, herb/drug interactions, listed on the basis of physiological effects; Appendix C, herbs contraindicated in mothers and children; and Appendix D, vitamin/mineral/drug interactions. Appendix A is subdivided into herbs that have a potential to produce allergic response, photosensitization, local irritation, acute inflammation of the urinary tract, irritation to the gastrointestinal tract, herbs that can affect the thyroid, and herbs that should only be used under the supervision of a healthcare provider due to their potential to produce serious adverse effects.

> **"Drug interactions per se are no threat to a patient; a physician's ignorance, either through lack of knowledge of interaction or through lack of adequate observation of the patient and proper interpretation of new events, is dangerous."**
>
> —Kenneth Lloyd Melmon and Howard Fred Morreli, 1978.

Appendix B includes herbs that can modify absorption, affect pharmacological activities, and herbs that interfere with distribution, clearance, and elimination. Appendix C includes herbs that should be avoided during pregnancy, while breast-feeding, and in children. Appendix D includes interactions between drugs and minerals with vitamin supplements.

The number of references has been expanded to a total of 1,099 citations. The author has highlighted significant references in the reference list. Five free web updates to the text will be available at <www.electicherb.com>. The updates are intended to supplement the third edition so that users will not have to purchase a new printed edition annually, and should be a godsend to those interested in the latest information on herb contraindications and drug interactions.

Several key elements should be considered when evaluating information sources on herbal medicine. For instance, one should consider the reputation of the author, whether the information is unbiased, if the information referenced, and how often the reference is updated. Of particular importance, the author should evaluate the strength and validity of the evidence.

The author, Francis Brinker, N.D. is a well-known and respected authority in herbal medicine. The first two editions of the book have been highly praised. The information in this edition is current, thorough, and detailed enough to be useful when needing quick information. The soft-cover book, albeit a little bulky, will fit in a lab coat pocket. The web updates will be well worth the minimal price of the book.

Healthcare practitioners need to know the strength of the evidence supporting the key clinical recommendations. The United States Pharmacopoeia (USP) has established criteria to evaluate the literature on the efficacy and safety of herbal supplements. The USP has classified four levels of evidence. Level I consists of "high quality" randomized controlled trials, meta-analysis, or epidemiological studies. Level II includes randomized controlled trials, meta-analysis, or epidemiological studies that have methodological flaws. Level III includes non-randomized studies, and Level IV includes case reports. The USP has concluded that only Level II evidence should be used to support an appropriate clinical decision.

The author has developed his own evidence-based system consisting of four categories of supporting research. Accordingly, category I of the book would include all four levels of the USP criteria. Therefore, category I of the book is too broad and should be subdivided. As an example, category I could be divided into category IA ("well conducted" clinical trials, meta-analysis, epidemiological studies), IB (less-well conducted clinical trails, meta-analysis, epidemiological studies), IC (non-randomized studies), and ID (case reports).

The author does not include the plant authority with the scientific binomial name which would help solve identification problems. Occasionally, the appendices are not in alphabetical order. Even though the author includes more than 600 herbs, a few commonly used herbs are not included (e.g., French maritime pine bark, also called Pycnogenol®, and grape seed extract).

Even with these minor flaws, the book is an invaluable resource for all health professionals, especially pharmacists, who should be on the front line when promoting the responsible use of herbal medicines. This book belongs on the shelf of every pharmacy. The nominal cost should allow healthcare students to purchase the book for their libraries. Additionally, consumers will find the book useful to better evaluate their efficacious and safe use of herbal medicines.

—Mary Chavez, Pharm.D.
Director of Complementary and Alternative Medicine Research and Education
Midwestern University – Glendale

Catnip Contraindicated?

I was reading *HerbalGram* 54 and found the article on catnip being effective against mosquitoes interesting. I had read something about it in another herb magazine and was glad to read a more detailed account of the research.

However, I'd like to offer you the same caveat I gave the other magazine, namely that catnip is attractive to *all* species of cats, wild and domestic. There was nothing in either article that addressed this issue, which could be a significant problem to the commercial use of catnip derivatives as insect repellant. It would be bad enough to have every cat in your neighborhood follow you while you're out jogging, but it could be downright dangerous to go hiking in the mountains where larger species of cats make their homes.

Research has shown that one of the reasons catnip is so attractive to cats is that it seems to mimic the sex hormones given off by females in heat. Not exactly what you want to advertise when you're out for a walk in the woods.

Catnip given to big cats in zoos has shown that the euphoric reaction is common to all members of the cat family. A Siberian tiger gets just as crazy on catnip as the neighbor's tabby. Not a comforting thought to me.

I'm glad to see researchers working on finding herbal insect repellants but I'd be very careful about employing catnip until more research is done on what, if any effect the extract might have on members of the cat family, wild and domestic.

A. LaCroix
New Britain, CT

[*Editor's note: We turned to ABC Advisor Arthur O. Tucker, Ph.D., of Delaware State University, for response to this letter because of his extensive research into this very topic. His reply:*]

I have seen no research that says that nepetalactones are similar to "sex hormones given off by females in heat." Further, cats give off sex pheromones, maybe, but not hormones (some insect physiologists prefer restricting the term "pheromones" to insects and applying "social odors" to mammals).

Actually, we don't know why cats react. We have an unpublished hypothesis (because it needs supportive evidence), but all the reactions of the catnip response are displacement activities from behavior involving both sex and food (salivation is the first response, and my cats don't salivate over sex ... turkey coldcuts, yes, but not sex!).

Furthermore, of the family Felidae, cheetahs (*Acinonyx jubatus*) do not react, and even within the genus *Felis*, this is genetically determined. Some cats are unreactive, and reaction depends upon the social setting, as well. So, in short, not "all" cats react.

The broad-spectrum action against many insects was pointed out in my review paper on catnip and catnip response in *Economic Botany*.[1] What is news is, that relatively nontoxic catnip is better than the relatively toxic DEET. The idea here is that isomers similar to nepetalactones, but not attractive to cats, may be an alternative to DEET. Since there is currently no commercial producer of catnip oil with high nepetalactones, don't worry about somebody spraying catnip oil on your car at the wild animal park. However, this is a line of future research to find an alternative to DEET.

Reference:

1. Tucker AO, SS Tucker. Catnip and the catnip response. *Econ Bot* 1988;42:214-31.

Distributional Range Correction

Please refer to the article "New species may revolutionize anti-cancer medications" in *HerbalGram* 54. The author mentioned that *Camptotheca acuminata* is now also found in India. I have been associated with the raw materials of camptothecin since 1978 in India. *C. acuminata* does not grow in India in the wild nor under cultivation.

However, another plant, *Nothapodytes nimmoniana* (J. Graham) Mabb., Icacinaceae, syn. *Mappia foetida* (Wighr) Miers, from the western ghats of India contain camptothecin. All the parts of this tree contain camptothecin, methylcamptothecin, and mappicine. These alkaloids can be converted into camptothecin and, further, into the anti-cancer compounds, topotecan or irinotecan. The wood chips of this tree have been exported from India, mainly to Japan and some to the United States, since 1978. Quite a few Indian companies extract camptothecin and export the value-added product. The Indian company, Dr. Reddy's lab in Hederabad, launched the product with topotecan last year.

Nothapodytes nimmoniana syn. *Mappia foetida*.
Photo © 2002 V.R.Pusalkar

Yet another Indian plant contains camptothecin — a small herb *Ophiorhiza mungus* (Rubiaceae) — but it is a rare species in India and thus has not been exploited for this purpose so far.

I am cultivating *N. nimmoniana* on 40 hectares in collaboration with M/S Indena spa, Milan, Italy, since 1994. The plantation is now matured and in flowering/fruiting stage.

V.R. Pusalkar, Botanist
Aruna Planta Medica, Alagapuram
Salem, South India

Clearly, we accessed an unreliable database when gathering information for this article. We appreciate the correction. —Editor

Parts Is Not Parts

I have read with interest your article on the use of artichoke *leaf* extract (ALE) for irritable bowel syndrome [*HerbalGram 55*]. In the course of the article you mention the leaf, however, the picture you present is of the immature flower head. We eat the fleshy bases of the immature flower heads and the fleshy base of the large bracts. So I am trying to figure out if your picture is just a mistake or if you want us to believe that the parts of the artichoke that we eat and/or that are medicinal are the leaf or the flower head. It is a confusing picture/article. Please clarify. I am sure that you would not want your readers to think that if they ate the usual part of the artichoke, the flower head, that they would experience the relief from their complaints that they would have if they had the ALE.

In my experience, it is the leaf, and not the "choke" (flower) that is the stronger of the medicinal parts. The leaf is woolly and certainly not edible, but can be dried and used as tea for many herbal uses.

Jeanne Rose
Institute of Aromatic and Herbal Studies
San Francisco, California

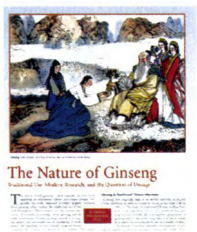
We appreciate Ms. Rose's clarification of the distinction between artichoke leaf and the immature flower (choke). The photo on page 16 of issue 55 was chosen as a graphic representation of the artichoke plant's most distinguishing feature, just as we might show a photo of the distinctive echinacea flower to illustrate an article on Echinacea purpurea *root. — Editor*

Kudo and Correction

Thank you for the positive review of our publication, the *Natural Dietary Supplements Pocket Reference*, which appeared in *HerbalGram* 54. We appreciate your affording INPR the opportunity to make this compact reference work known to the readers of *HerbalGram*. I'm certain that your review will do much to boost its visibility and wider distribution. The publication, which is intended to be a concise reference

summarizing key information on the more popular herbal supplements and does not pretend to be comprehensive, does seem to appeal to health care professionals, pharmacists, and others who find a handy, pocket-size "quick reference" of this sort useful in their daily activities.

I did want to mention that the companion volume to the Pocket Reference that is being published in the Spring of 2002 by the Haworth Herbal Press, will appear under a different title than the one quoted in your review. The new title is *Botanical Medicines: The Desk Reference for Major Herbal Supplements*. The *Desk Reference*, as its name implies, will be much more comprehensive than the *Pocket Reference*, at least for the 34 most popular herbal supplements that are covered in its monographs.



I would also like to take this opportunity to thank you, and the other members of the ABC/*HerbalGram* staff for the wonderful job that you do, on a budgetary shoestring and often under tight deadlines. *HerbalGram* and HerbClip are both invaluable tools that I use constantly in my own professional activities as well as in the course I teach on botanical medicines at the University of Minnesota. I recommend membership in ABC to all of my students and if I could make it a course requirement, I would do so! *HerbalGram* brings balance, comprehensibility, technical accuracy, cutting-edge science, and great graphic beauty on the subject of botanical medicines to a wide audience of both lay and professional people. I always read every issue from cover to cover and await the next one eagerly.

I honestly don't know how you manage to turn out such a high-quality and invariably fascinating publication, time after time; but however you do it, please keep doing it. The world needs more publications like *HerbalGram* and more dedicated people like the *HerbalGram*/ABC staff to enable people to understand, appreciate, and benefit from the abundance of botanical medicines that the world has to offer.

All my best wishes for your continued success.

Dennis J. McKenna, Ph.D.
Executive Director
Institute for Natural Products Research, and
Senior Lecturer
Center for Spirituality and Healing Academic Health Center
University of Minnesota

Concerning Regional Ginsengs and the Tortuous Taxonomy of the Genus *Panax*

The recently published omnibus article on ginseng (The Nature of Ginseng by S. Dharmananda, *HerbalGram* 54) I found interesting and informative in many respects, particularly in the area of tradirional Chinese medicine. However, I was arrested by photographs of Tienchi (Sanchi) ginseng taken by the author and respected herbalist/botanist Steven Foster, which designated the roots as deriving from *Panax pseudoginseng* var. *notoginseng*.

This species is most commonly encountered today as *P. notoginseng* (Burkill) F.H. Chen, as in Court's recent book, *Ginseng: The Genus* Panax.[1] Court acknowledges the work of Wen and Zimmer,[2] who clarified the complex and, historically, often complicated and revised taxonomy of *Panax*, using sequences of the internal transcribed spacers (ITS) and the 5.8S coding region of the nuclear ribosomal DNA repeat. Wen (at the time associated with the Laboratory of Molecular Systematics at Colorado State University) and Zimmer (of the Department of Botany at the National Museum of Natural History, Smithsonian Institution in Washington, D.C.) settled upon 12 species. Later, Wen (now at the Field Museum of Natural History in Chicago) published a revised taxonomy, which recognizes 11 species and one variety,[3] and includes the most recently characterized species, *P. vietnamensis* Ha & Grushv. (Vietnamese ginseng), which replaced *P. omeiensis* J. Wen and *P. sinensis* J. Wen. In this latest taxonomic revision, *P. bipinnatifidus* Seemann (synonymous with *P. pseudoginseng* Wall. var. *bipinnatifidus* (Seemann) Li and *P. pseudoginseng* Wall. ssp. *himalaicus* Hara) replaces *P. major* Ting, and *P. bipinnatifidus* Seemann var. *angustifolius* (Burkill) J. Wen (synonymous with *P. pseudoginseng* Wall. var. *angustifolius* (Burkill) Li) is included as formerly *P. sikkimensis* Banerjee. Wen has also altered the authority attaching to Sanchi/Tienchi ginseng as *P. notoginseng* F.H. Chen ex C.Y. Wu & K.M. Feng.

Curiously, *HerbalGram* and AHPA's 2nd edition of *Herbs of Commerce* (*H of C*) use the long outdated *P. pseudoginseng* var. *notoginseng* G. Hoo & C.J. Tseng, *H of C* actually citing as synonymous, *P. notoginseng* (Burkill) F.H. Chen ex C.Y. Wu & K.M. Feng. Oddly also, *H of C* gives priority to *P. pseudoginseng* var. *japonica* (C.A. Mey.) G. Hoo & C.J. Tseng, for Japanese ginseng, long recognized as *P. japonicus* C.A. Mey., which *H of C* relegates to synonymy; Wen,[3] as did Wen and Zimmer,[2] recognizes *P. repens* Maxim as the most prominent synonym for *P. japonicus*, but the former author lists also *P. quinquefolia* b. *japonica* Siebold. Himalayan or Nepalese ginseng is *P. pseudoginseng* Wall.

It is absolutely imperative when reviewing literature on *Panax* species that one be thoroughly conversant with the historical taxonomy of the genus, because very few researchers are punctiliously attentive to this aspect of herbal scientific research. The exhortation of the late Professor Varro Tyler[4] that careful attention be paid to the Latin taxonomic *authority*, in order to ensure correct botanical identification of plant material to be subjected to clinical evaluation, is abundantly supported by the taxonomic odyssey of this singular genus, here briefly excerpted.

Dennis V.C. Awang, Ph.D., F.C.I.C.
MediPlant Consulting Inc.
White Rock, British Columbia, Canada

Reference:

1. Court WE. *Ginseng: The Genus* Panax. Amsterdam: Harwood Academic Publishers; 2000.
2. Wen J, Zimmer EA. Phylogeny and biogeography of *Panax* L. (the ginseng genus, Araliaceae): Inferences from ITS sequences of nuclear ribosomal DNA. *Molecular Phylogenetics and Evolution* 1996;6(2):176-7.
3. Wen J. Species diversity, nomenclature, phylogeny, biogeography, and classification of the ginseng genus (*Panax* L. Araliaceae). in: Punja ZK, editor. *Utilization of biotechnological, genetic and cultural approaches for North American and Asian ginseng improvement*, Proceedings of the International Ginseng Workshop 2001 Simon University Press, Vancouver, Canada. pp. 67-88.
4. Tyler VE. Product definition deficiencies in clinical studies of herbal medicines. *Scientific Review of Alternative Medicine* 1999;4(2):17-21.

HerbalGram *relies upon* Herbs of Commerce, *2nd edition, as a primary resource for plant names. Herbs of Commerce is the authoritative source for common names and is a preliminary reference for Latin binomials, in need of additional verification. Regarding Latin binomials, the introduction of that book states, "... status ... [of these] are prone to revision from time to time." [pp. xv]*

The editors of Herbs of Commerce *agree with the concerns raised by Dr. Awang, and their reference — the U.S. Department of Agriculture's Agricultural Research Service Germplasm Resources Information Network (ARS GRIN) database — has been modified to reflect this information.— Editor*

HerbalGram welcomes letters to the editor as part of the ongoing dialog that makes science so vibrant, and as part of our efforts to learn as well as to educate. Please submit your letters to Karen Robin, managing editor, via email <krobin@herbalgram.org>, or by postal service in care of the American Botanical Council, P.O. Box 144345, Austin, TX 78714-4345, USA. Be sure to include your contact information so we may confirm.

The editors reserve the right to edit, clarify, or decline to publish.

2002

November 1–3: Integrative Cancer Therapies Symposium. Evanston, IL. Presented by the University of Illinois at Chicago College of Medicine and The Institute for Integrative Cancer Research and Education. 40+ speakers scheduled. Contact: Genevieve Hedland, ICT Symposium Office. Ph: 888/753-7001. E-mail: <ghedland@bacon-hedland.com>.

November 1–4: World Ayurveda Congress, Kochi, Ernakulam, Kerala, India. Organized by Swadeshi Science Movement, a unit of Vijnana Bharati, in association with Ministry of Health & Family Welfare Govt. of India Congress. Contact: Secretary General, World Ayurveda Congress 2002, Post Box No: 28, Thiruvananthapuram-695001, Kerala, India. Ph: +91/471 460055. E-mail: <mail@ayurworld.org> <aycongress@hotmail.com>. Website: <www.ayurworld.org>.

November 1: Application deadline for UCSC Farm & Garden Apprenticeship, Santa Cruz, CA. Intensive 6-month course in organic gardening and small-scale farming. 35-40 trainees; UCSC is especially interested in increasing the diversity of applicants. Contact: Erin Barnett, Apprenticeship Coordinator, CASFS, UCSC, 1156 High Street, Santa Cruz, CA 95064. Ph: 831/459-3240. E-mail: <apprenticeship@cats.ucsc.edu>. Website: <www.ucsc.edu/casfs>.

November 2–3: Ontario Association of Naturopathic Doctors Annual Convention: Clinical Evidence in the 21st Century, Burlingron, Ontario, Canada. Contact: OAND, 344 Bloor St. W, Ste. 602, Toronto, ON M5S 3A7 Canada. Ph: 416/233-2001 ext. 40; fax: 416/233-2924. Email: <info@oand.org>.

November 6–8: 4th Annual Congress on Traditional Medicine, Lima, Peru. Organized by the Colegio Médico del Perú. Topics include ethnobotany, ethnopharmacology, phytotherapy and more. Contact: Barbara Johnston. Ph/Fax: 464-13-168; E-mail: <cimt@terra.com.pe>.

November 7: Distinguished Lectures in the Science of Complementary and Alternative Medicine, Bethesda, MD. Arthur Kleinman, M.D., Professor of Social Anthropology, Harvard University, and Maude and Lillian Presley Professor of Medical Anthropology and Psychiatry, Harvard Medical School, will present "The Global Transformation of Health Care: Cultural and Ethical Challenges to Medicine." Ph: 301/594-9632.

November 7–10: Natural Products Organic Asia, Singapore. Congregates manufacturers, suppliers, distributors, agents, industry professionals and buyers from all over the world. Contact: Ms. Sylwin Angdrew, Senior Marketing Executive. Ph: (65) 6534-3588; fax: (65) 6534-2330. Email: <aylwin@hqlink.com>.

November 8-16: Incan Healers/Shamans Workshops. Colorado area. Amazonian Cosmology of "Ayahuasca" as a time-space medicine will be the focus of this workshop. Contact: Ed and Tania Tuttle. Ph: 612/ 825-3792. E-mail: <shaman@sacred-journey.com>. Website: <www.sacred-journey.com>.

November 8-16: Shamanic Journeys to the Ecuadorian Andes, Amazon, and Pacific Ocean. Contact: Ed and Tania Tuttle. Ph: 612/825-3792. E-mail: <shaman@sacred-journey.com>. Website: <www.sacred-journey.com>.

November 9: Festival Hill's Herbal Seminars series: Creating a Garden of Your Own. Round Top, TX. Seminar includes buffet luncheon, printed materials and supplies, tastings, garden tour and plant treasures. $60 per person. Contact: The Herbal Forum at Round Top, P.O. Box 23 Round Top, Texas 78954. Ph: 979/249-3973. Fax: 979/249-3961. Other seasonal seminars set for Dec. 4 & 7, Feb. 22 & 23, Mar. 4, Apr. 8 & 23, May 10.

November 9–10: Green Festival. San Francisco, CA. Promotes sustainability of local green economies by fostering fair trade and fair wage practices, environmental responsibility, localized cooperation, community building and accountability. Produced by Global Exchange, Co-op America and Bioneers. Ph: 877/727-2179. Email (for those interested in exhibiting): <exhibit@greenfestivals.com>. Website: <www.greenfestivals.com>.

November 12-13: International Symposium on Modern Technology in Chinese Herbs-Quality Control, Taichung, Taiwan. Sponsored by the Ministry of Education. Contact: China Medical College, Institute of Chinese Pharmaceutical Sciences. Ph: 886-4-2203-0380. Fax: 886-4-2208-3362. E-mail: <yschang@mail. ccmc.edu.tw>.

November 14-17: Indigenous Healing Traditions of the Americas: Paths to a New Medicine. Washington, DC. Explore the uniqueness, wealth and complexity of healing traditions indigenous to the American continents, with emphasis on their potential for delivering culturally sensitive and effective health care. Contact: Marisol Villanueva, Pro Cultura, P.O. Box 185, Pleasantville, NY 10570. Ph: 866/547-3309. Fax: 317/328-1475. E-mail: <mail@procultura.org>. Website: <www.procultura.org>.

November 16: Herb Days at Festival Hill. Round Top, TX. Tours begin at 11am with luncheon and lecture and last until 2pm. $30 per person. Contact: The Herbal Forum at Round Top, P.O. Box 23 Round Top, Texas 78954. Ph: 979/249-3973. Fax: 979/249-3961. Also on Dec. 10, Mar. 12, Apr 16 & 30, May 14.

November 17–20: Worldnutra 3rd Annual Conference and Exhibition on Nutraceuticals and Functional Foods: "From Laboratory to the Real World and the Marketplace," San Diego, CA. Ms. Nedra Sneed, Conference Secretary, Worldnutra, P. O. Box 10506, College Station, TX 77842. Ph/fax: 979-846-1951. Email: <nutra@tca.net>; website: <http://www.worldnutra.com/>.

November 27–30: 2002 World Neem Conference: Neem for Sustainable Development, Mumbai, India. Sustainable agriculture, human and animal health, constraints facing Neem industry, processing and more. Contact: Neem 2002 Secretariat, 67-A, Vithalanagar Society, Road # 12, Juhu Scheme, Mumbai – 400 049, India. Fax: +91 22 620 7508. Email: <wncregistration@neemfoundation.org>.

December 4: Current Issues with Dietary Supplements: Safety, Toxicology and California Proposition 65, Venetian Conference Center, Las Vegas, immediately before SupplySide Wesr. Expert panel to discuss botanical and ingredient safety issues, dietary supplement product liability and risk assessment, the impact of food safety security legislation, and effects of adverse event reporting. Sponsors include American Herbal Pharmacopoeia, American Herbal Products Association, AOAC International, Consumer Healthcare Products Association, Council for Responsible Nutrition, Institute for Nutraceutical Advancement, National Nutritional Foods Association, ChromaDex, Virgo Publishing, and the Center for Public Health Education. More information at www.nsf.org/cphe/ds <http://www.nsf.org/cphe/ds> , phone 800/NSF-MARK ext. 5723.

Dec. 4-6: Virgo Publishing's SupplySide West. The Venetian, Las Vegas. Share new science or research with a room full of industry execs. Contact: 480/990-1101. Website: <www.supplysideshow.com>

December 8-12: Cucurbitaceae 2002 Conference, Naples, Italy. Contact: Don Maynard or Beth Miller-Tipton. Fax: +1/352/392-9734. E-mail: <bmiller-tipton@mail.ifas.ufl.edu>.

2003

January 8–11: International Society for Ethnopharmacology and South African Association of Botanists International Conference, Pretoria, South Africa. How ethnobotany and ethnopharmacology can bridge the gap between traditional knowledge and sustainable development. Main topics: the treatment of infectious diseases, plants in the community, conservation and sustainable use, and biological and chemical studies. Website: <http://www.ethnopharmacology.org/ISEhomepage.html>.

January 9-18: Ayahuasca Healing Retreat. Lectures, four ayahuasca ceremonies and two *Salvia divinorum* ceremonies, group sharing, creative artwork expression, biofeedback, transpersonal exercises and excursions. Contact: Silvia Polivoy, Av. Kennedy 2842 6a, 1425 Buenos Aires, Argentina. Ph/Fax: (54-11) 4774-3892. Email: <Silviap@house. com.ar>, Website: <www.ayahuasca-healing.net>.

January 21-24: Functional Beverage Summit 2003. Seattle, WA. The summit will include programs on marketing and R&D as well as more scientific presentations and speakers from Europe, Asia, Australia and Latin America. Website: <www.foodbevx.com>.

February 3–7: 3rd World Congress on Medicinal and Aromatic Plants for Human Welfare (WOCMAP III), Chiang Mai, Thailand. Contact: Dr. Araya Jatisatienr, Chiang Mai University, Dept. of Biology, Faculty of Science, Chiang Mai 50202, Thailand. Ph: +66 53 943346 or 943348, fax: +66 53 892259, email: <secretariat @wocmap.org>, website: <http://www. wocmap3.org>.

February 28-March 7: 7th Annual AromaHerb Conference and Trade Show, Tempe, AZ. Leading companies in the essential oil industry, worldwide essential oil distillers, renowned herbalists and authors. Approximately 50 presenters and 100 companies. Exhibiting only pure and natural products. Ph: 602/938-4439, Email: <aromaherbshow@hotmail.com>.

March 22: The 8th Annual Herbal Forum at Round Top. Round Top, TX. A Celebration of Herbs Featuring Basil, Herb of the Year 2003! Includes lectures, demonstrations and exhibits, extensive herbal book store, garden buffet luncheon and afternoon tea, giant plant sale, more. Optional workshops March 21. Contact: The Herbal Forum at Round Top, P.O. Box 23 Round Top, Texas 78954. Ph: 979/249-3973. Fax: 979/249-3961.

March 28-April 1: APhA Annual Meeting. New Orleans, LA. Titles and 200-word abstracts for 15-minute podium presentations deadline Oct. 1, 2002. Contact: Michael Montagne, 179 Longwood Ave, Boston, MA 02115. Ph: 608/262-5378. E-mail: <mmontagne@mcp.edu>.

April 6-9: PhytoChemistry and Biology of Lignans, Conference Center Walberberg, Germany. Contact: Prof. Maike Petersen, Institute for Pharmaceutical Biology, Philipps-Universtat Marburg, Deutschhausstr. 17A, D-35037 Marburg, Germany. Ph: 49-(0)6421-2825821, Fax: ++49-(0)6421-2825828, Email: <petersen@mailer.uni-marburg.de>, Website: <www.lignans.de>.

April 14-October 17: UCSC Farm & Garden Apprenticeship, Santa Cruz, CA. Intensive 6-month course in organic gardening and small-scale farming. 35-40 trainees; UCSC is especially interested in increasing the diversity of applicants. Application deadline is Nov. 1, 2002. Contact: Erin Barnett, Apprenticeship Coordinator, CASFS, UCSC, 1156 High Street, Santa Cruz, CA 95064. Ph: 831/459-3240. E-mail: <apprenticeship@cats.ucsc.edu>. Website: <www.ucsc.edu/casfs>.

April 30: Herb Days at Festival Hill. Round Top, TX. Tours begin at 11am with luncheon and lecture and last until 2pm. $30 per person. Contact: The Herbal Forum at Round Top, P.O. Box 23 Round Top, Texas 78954. Ph: 979/249-3973. Fax: 979/249-3961.

May 5-7: Virgo Publishing's Supply Side East. Meadowlands Exposition Center, Secaucus, N.J. Share new science or research with a room full of industry execs. Contact: 480/ 990-1101. Website: <http://www.supplysideshow.com/>

May 8-10: 5th Coloquio Europeo de Etnofarmacologia Congreso Internacional. Valencia, Spain. The program will focus on cultural inbreeding in ethnopharmacology. Contact: Blasco Ibanez, 15, 46010 Valencia, Spain. Ph: (00)34+963-86-47-64 Fax: (00)34+963-61-39-75. Website: <www.uv.es/Etnofarmacologia/>.

May 10: Festival Hill's Herbal Seminars series: Razzle, Dazzle Basil Fest! Round Top, TX. Includes buffet luncheon, printed materials and supplies, tastings, garden tour and plant treasures. $60 per person. Contact: The Herbal Forum at Round Top, P.O. Box 23 Round Top, Texas 78954. Ph: 979/249-3973. Fax: 979/249-3961.

May 14: Herb Days at Festival Hill. Round Top, TX. Tours begin at 11am with luncheon and lecture and last until 2pm. $30 per person. Contact: The Herbal Forum at Round Top, P.O. Box 23 Round Top, Texas 78954. Ph: 979/249-3973. Fax: 979/249-3961.

May 14-18: All Things Organic 2003, Austin, TX. The Organic Trade Association is the membership-based business association representing all sectors of the organic industry throughout North America, and it encourages global sustainability through promoting and protecting the growth of diverse organic trade. Contact: Lori Wyman, IGC 2003, PO Box 547, Greenfield, MA 01302, Ph: 413/774-7511, ext.11; fax: 413/774-4432. Email: <lwyman@ota.com>. Website: <www.ota.com>

May 3–5: International Symposium on the Role of Botanicals in Aging, New Brunswick, NJ. Presented by the American Herbal Products Association & Rutgers University. Confirmed speakers include Jim Duke, Ph.D., and Jerry Cott, Ph.D. CEUs offered. Contact: Natasha Hall, AHPA, 8484 Georgia Ave Suite 370, Silver Spring, MD 20910. Ph: 301/588-1171. Email: <nhall@ahpa.org>.

June 27-29: 66th Annual Natural Products Convention and Trade Show. Las Vegas, NV. Contact: NNFA, 3931 MacArthur Blvd, Ste 101,Newport Beach, CA 92660. Ph: 800/966-6632. Website: <.www.nnfa.org>.

Oct. 1-3: Virgo Publishing's SupplySide West. Venetian Hotel and Sands Exposition Center, Las Vegas. Share new science or research with a room full of industry execs. Contact: 480/ 990-1101. Website: <www.supplysideshow.com>.

November 27–30: International Ginseng Conference: The Globalization of Ginseng, Melbourne, Victoria, Australia. Organized by the Australian Ginseng Growers Association. Includes trade and poster displays, technical program, and post conference tours. Contact: Conference Secretary, IGC 2003, PO Box 250, Gembrook, Victoria 3783, Australia. Ph: 61 3 5968 1877; fax: 61 3 5968 1119. Email: <agga@nex.net.au>.

Access

International Symposium on the Role of Botanicals in Women's Health proceedings document is now available from the American Herbal Products Association (AHPA). This February 2002 symposium focused on fundamental impact of botanicals on a variety of women's health conditions, clinical observations made by leading practitioners, and emerging scientific research on red clover, black cohosh, chaste tree, and soy. $100 + S/H. Contact: Natasha Hall, AHPA. Ph: 301/588-1171 x106. Email: <nhall@ahpa.org>.

Phytochemistry Reviews, a new journal containing the proceedings of the Phytochemical Society of Europe, offers both paper and online subscriptions. Contact: Kluwer Academic Publishers. Ph: 866/269-9527. Email: <kluwer@wkap.com>. Website: <www.kluweronline.com>.

www.Herbalchem.net is a new website on herbal phytochemistry for the herbalist/practitioner, general public, health food/supplement store staff, and others. Information available on Introductory, Intermediate, and Advanced levels.

Plants Personified announces a limited time offer on some of its publications, including Ginseng, Plant Biotechnology, and Plant Medicinals. Each volume facilitates technical understanding of a subject's past and its future potential. Contact Plants Personified, Inc, P.O. Box 18582, Eastside Station 1600 18th Ave, NE, Minneapolis, MN 55418. Email: <ppinc111@msn.com>.

Jeanne Rose Aromatherapy Seminars include distillation, blending, rare perfumery, and foundations of aromatherapy and essential oils. Learn from this master herbalist and aromatherapist in Reno (Oct. 25-27); Pottstown, PA (Nov. 15-17); and San Francisco (Feb. 21-23). Contact: Jeanne Rose. Ph: 415/564-6785. Email: <info@jeannerose.com>.

Gene Conserve is an electronic journal devoted to conservation of crop genetic resources with emphasis on cassava. Contact: Gene Conserve Website/E-mail: <students@econbot.org>. Website: <www.geneconserve.pro.br>.

The Natural Heritage journal is available online. Website: <www.thenaturalheritage.com>.

American Association of Homeopathic Pharmacists' new website provides accurate information regarding the legal status of homeopathy, and reputable manufacturers of homeopathic drug products. Contact: Eric L. Foxman, Secretary, AAHP, 3741 Mitford Lane, Clinton, WA 98236. Ph: 800/478-0421. <www.homeopathicpharmacy.org>.

Herbal Medicines Safety Advice is available from the United Kingdom's Medicines Control Agency website, including herb/drug interactions, safety concerns raised by other agencies, quality control alerts, and details of contamination or wrongful inclusion of ingredients. <www.mca.gov.uk/ourwork/licensingmeds/herbalmeds/herbalsafety.htm>.

The New York Botanical Garden's Fall 2002/Winter 2003 catalog includes hundreds of classes in seven disciplines: botanical art and illustration, botany, commercial horticulture, floral design, gardening, horticultural therapy, and landscape design. The largest and most diverse continuing education of any botanical garden. Contact: Leeann Lavin. Ph: 718/817-8743. E-mail: <llavin@nybg.org>. <www.nybg.org/edu/conted>

The Pharmacopoeia of the People's Republic of China (2000 English Edition), the Chinese Pharmacopoeia Commission's official and authoritative compendium of drugs, covers traditional Chinese medicines and most Western medicines and preparations. Contact: Chi Zhenguo, Rm. 604, Bldg. 7, Qian Hai Hua Yuan, Tao Yuan West Rd., Nantou, Nanshan, Shenzhen, Guangdong, P.R. China 518052. Fax: +86 755 26161829 E-mail: <szchis@public.szptt.net.cn>. <www.tradezone.com/tradesites/chizhenguo.html>.

Alternative Perspectives, the newsletter of the National Foundation for Alternative Medicine, is available online and in PDF format. NFAM seeks to inform about the scientific potential of CAM to treat chronic diseases, in particular, cancer. Website: <http://www.nfam.org>.

Current Topics in Nutraceutical Research, a new scientific journal for the nutraceutical industry is scheduled to launch December 2002. This is international, interdisciplinary broad-based peer-reviewed journal offers critical evaluation of research on nutraceuticals. <www.nutraceuticalresearch.org>

NatureServe is a non-profit organization dedicated to providing knowledge to protect the natural world. Formerly the Association for BioDiversity Information (ABI), NatureServe works with The Nature Conservancy to help meet local, national, and global conservation needs, and helps to guide conservation decision-making and sound land use planning. Contact: NatureServe, 1101 Wilson Blvd, 15th Floor, Arlington, VA 22209. Ph: 703/908-1800. Website: <www.natureserve.org>.

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Correspondence Courses And Seminars

Aromatherapy and Herbal Studies Course/Jeanne Rose. Correspondence, certification, in-person intensives. 160 CEU provided, California Board of RN Provider #CEP11659. Info: 219 Carl St., San Francisco, CA 94117 or FAX 415/564-6799.

Foundations in Herbal Medicine by Tieraona Low Dog, MD, AHG, is a video and text-based Correspondence Course in Herbal Medicine with over 700 pages of text and almost 60 hours of video. Dr. Low Dog is a past president and founding member of the American Herbalist Guild. For more information, visit our website (fihm.com) or call 888-857-1976 for a free syllabus.

Publications

American Herb Association Quarterly Newsletter — $20/yr. AHA, P.O. Box 1673, Nevada City, CA 95959.

Australian Journal of Medical Herbalism — quarterly publication of the National Herbalists Association of Australia (founded in 1920). Deals with all aspects of Medical Herbalism, including latest medicinal plant research findings. Regular features include Australian medicinal plants, conferences, conference reports, book reviews, rare books, case study and medicinal plant review. AUD/$95 plus AUD/$15 if required by airmail. National Herbalists Association of Australia, 33 Reserve Street, Annandale, NSW 2038, Australia.

HerbalGram — Quarterly journal published by the American Botanical Council. A benefit at all levels of membership in ABC. See page 3 for membership information or join online at <www.herbalgram.org>. P.O. Box 144345, Austin, TX 78714. 800/373-7105 or fax 512/926-2345. Email <abc@herbalgram.org>.

Medical Herbalism — Subtitled "A Clinical Newsletter for the Herbal Practitioner." Edited by Paul Bergner. $36/yr, $60/2 yrs. Canada $39/yr. Overseas $45/yr. Sample/$6. Medical Herbalism, P. O. Box 20512, Boulder, CO 80308.

Wildflower — North America's only popular magazine devoted solely to the study, conservation, cultivation, and restoration of our continent's native flora. Offering an appealing blend of art and science, this 52-page quarterly examines all aspects of popular botany in North America from the rain forests of Panama to the mosses of the Arctic tundra; from gardening with native trees, shrubs, wildflowers, and ferns to the latest projects in habitat and native plant conservation. The green revolution begins in our own backyard. Subscriptions and membership are $35/1 yr., $70/2 yrs. Sample copy $9. To subscribe, order from website: <www.wildflowermag.com> or by mail: Wildflower Subscriptions, Box 335 Station F, Toronto, ON Canada M4Y 2L7.

Schools

Aromatic Plant Medicine Diploma Course, with Jade Shutes and the Institute of dynamic Aromatherapy. Other educational material is available. For a brochure: 360/651-9809 or email <info@theida.com>.

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Herbal Education - Rocky Mountain Center for Botanical Studies, offering a diverse curriculum with over 20 herbal mentors. Comprehensive one-, two- and three-year programs - Education for life. Recommended by leading herbalists. Colorado State Certified. Call 303/442-6861 for brochure. RMCBS, Inc., PO Box 19254, Boulder, CO 80308. <rmcbs@indra.com> <www.herbschool.com>.

The International Institute of Traditional Herbal Medicine and Aromatherapy – offers an internationally accredited Residential Diploma Course in Aromatherapy and Therapeutic Massage in Provence, France, starting June 2002. Includes the science and energetics of 75 essential oils and educational tours of the region's aromatic delights. 01144-120-639-3465 <www.aromatherapy-studies.com>.

White Pine Healing Arts – Comprehensive 3-year program in Chinese Herbology, including academic and clinical components. Certification at professional level. Excellent faculty, all trained in China and able to read Chinese source texts. Accessible format. Distance learning options. 413/549-4021 <www.whitepinehealingarts.com> email <sweiz@ren.com>.

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Hawaiian Herbal Education — Go beyond rraditional herbalism to learn Hawaiian plant medicine secrets. 3-day hands-on workshops at Hi'iaka's Healing Hawaiian Herb Garden near Hilo. Scheduled for January, April, July, October 2003. Individual retreats also designed, scheduled upon request. $110/day includes lodging on-site. Details and images at <www.hiiakas.com>. Phone 808/966-6126, email <goddess@hiiakas.com>.

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Dear Reader

Continued from page 8

ally ignored by the media.

***Wall Street Journal* Article.** Perhaps the nadir of the present herb crisis is a highly misleading article in the August 29 issue of the *WSJ* by Chris Adams, "More Research Is Questioning Safety, Effectiveness of Herbs." The article mischaracterizes the state of the science regarding at least five top-selling herbs: ginkgo, SJW, SP, echinacea, and garlic, and included this astonishing statement, "Indeed, research has found that half of the dozen top-selling herbal supplements are either useless for their marketed purposes or dangerous." ABC's letter to the editor in response was not published; however it is available online <www.herbalgram.org/browse.php?content_name=press20020902>.

Herbs for Menopause. But, where's the good news, if any? The best comes in the aftermath of NIH's pulling the plug on a long-term trial hormone replacement therapy due to cardiovascular and cancer risks. Numerous articles in the *New York Times*, *WSJ*, and *Washington Post* noted that research supports the effects of black cohosh, red clover, and soy to reduce symptoms associated with menopause. ABC posted a new black cohosh monograph on our website <www.herbalgram.org/browse.php?content_name=Press20020918>.

Lack of space here prohibits mention of other good news: a new French study on SJW shows it *does* work in depression; butterbur for allergies, more on hawthorn for early heart disease, and so much more. Bright prospects in an otherwise bleak summer.

Bottom line. Just as there are legitimate concerns about quality control and safety with some products, there are also problems in the way the media *reports* on herbs. Many reporters have scant knowledge of the subjects they cover and biases against their subjects. The public deserves high quality, safe and effective herbal products for their health care. They also deserve straightforward, balanced, responsible reporting on the safety and benefits of these products.

Mark Blumenthal

Herbal Education Catalog

Inside This Catalog

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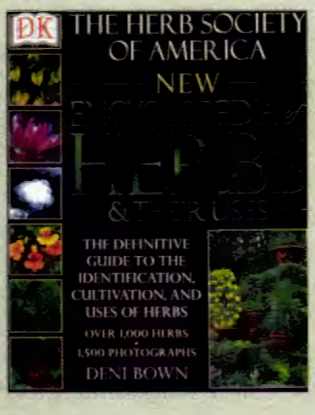

New Encyclopedia of Herbs and Their Uses

NEW EDITION

by Deni Bown. 2001. 2nd edition. The Royal Horticultural Society's new edition of the most comprehensive illustrated encyclopedia of herbs. More than 1000 species, varieties, hybrids, and cultivars listed alphabetically by genus. Addresses culinary, medicinal, and economic properties of each herb along with cultivation information. More than 1,500 color photographs by the author. Hardcover, 456 pp. $40. #B156

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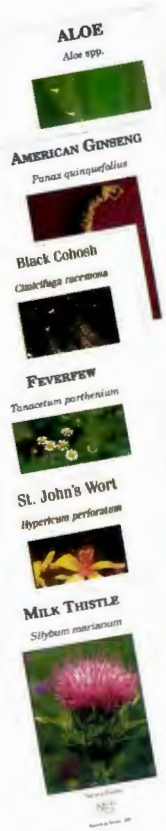
HerbalEducationCatalog

The Herbal Education Catalog is back by popular demand. You will note that it is smaller and the number of items offered is fewer. This is, in part, a cost consideration. What we have listed here are newer items and the essentials — books and monographs that anyone interested in herbal medicine should have in their library. We have more items on our website: sale books, closeout items, and special reports. Check them out at **www.herbalgram.org** or contact us for a list of what is available.

Don't forget that if you are a member of the American Botanical Council, you get a 5% discount on your purchases from our catalog and website. For information on membership, see page 2 of this issue of *HerbalGram*.



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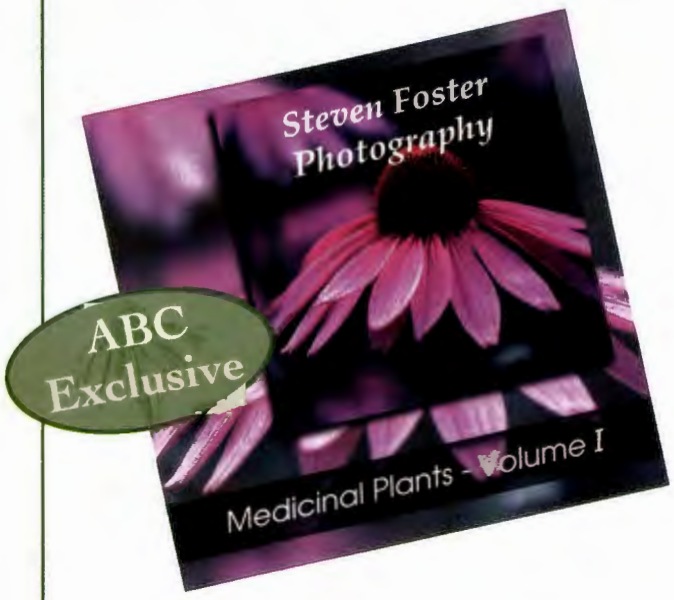

Steven Foster Photography

Medicinal Plants - Volume 1 CD-ROM

This royalty-free CD ROM contains 102 photos of some of the most popular medicinal plants in use today. Medicinal Plants - Volume I is designed for both Macintosh™ and Windows™ operating systems. The images are high resolution: 8x12 inches at 300 dpi (20.3x30.5 cm at 118 dpcm) and have excellent highlight and shadow detail.

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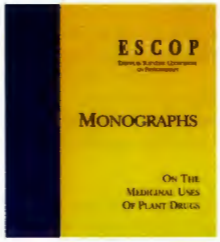

ESCOP Monographs

Prepared by the European Scientific Cooperative on Phytotherapy (ESCOP), a group of herbal experts from academia and industry in the European Union. These monographs contain indications, contraindications, side effects, dosage, interactions, and many other important therapeutic parameters of 60 leading herbs and phytomedicines in Europe. Well referenced. A must for physicians, pharmacists, naturopaths, herbalists, industry, and researchers.

ESCOP monographs are published in looseleaf form, for insertion into a dedicated ring binder. ESCOP employs the traditional pharmacopeial name of the herb as the title of each monograph.

For a complete listing of monographed herbs and fascicule divisions, visit our website: www.herbalgram.org/monographs.html

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WHO Monographs on Selected Medicinal Plants, Vol. 1

by the World Health Organization. 1999. Collection of 28 monographs covering the quality control and traditional and clinical uses of medicinal plants selected for inclusion on the basis of their widespread use, particularly in countries that rely heavily on medicinal plants to meet primary health care needs. Aims to encourage standardized scientific approaches to ensuring the safety, quality, and efficacy of medicinal plants and their products. Softcover, 287 pp. Item #428

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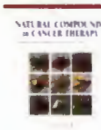

Natural Compounds In Cancer Therapy: Promising Nontoxic Antitumor Agents from Plants and Other Natural Sources by John Boik. 2001. Presents a solid scientific basis for the use of natural compounds in cancer treatment. Includes in-depth discussions of cancer at the cellular level and the level of the organism, as well as clinical considerations covering trace metals, vitamin C and antioxidants, polysaccharides, lipids, amino acids and related compounds, flavonoids, nonflavonoid phenolic compounds, terpenes, lipid-soluble vitamins, and the effects of natural compounds on chemotherapy and radiation therapy. Softcover, 521 pp. $32. #B494

Clinical/Therapeutic

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Botanical Influences on Illness by Melvin Werbach, M.D. & Michael T. Murray, N.D. 2000. 2nd Edition. Reviews of botanical treatments for 60 different illnesses. Materia medica on 26 common phytomedicines and annotated list of resources. Hardcover, 622 pp. $59.95 #B074

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The Complete German Commission E Monographs—Therapeutic Guide to Herbal Medicines Ed. by M. Blumenthal, W. Busse, A. Goldberg, J. Gruenwald, T. Hall, C. Riggins, and R. Rister. 1998. The official English translation of the monographs resulting from the German Federal Health Agency's expert committee. The 2nd-ranked medical book of 1998 (Doody Publishing). Contains 380 monographs, 190 herbs and fixed combinations approved for therapeutic use, 150 indications, and more. Hardcover, 685 pp. $89. #B181. CD-ROM $49. #C181

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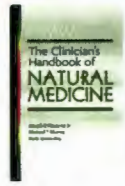
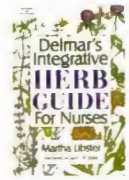
Herbal Medicine: Expanded Commission E Monographs Ed. by M. Blumenthal, A. Goldberg, and J. Brinckmann. 2000. Expanded content on the Commission E herb monographs for the most widely used herbs in the U.S. Includes updated, detailed information on their botany, history, chemistry, pharmacology, safety, efficacy, and therapeutic use. Extensive list of published references. Hardcover, 519 pp. $39.95. #B181E. CD-ROM $39.95. #C181E

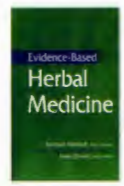


The Clinician's Handbook of Natural Medicine by Joseph Pizzorno Jr., Michael Murray, and Herb Joiner-Bey. 2002. Provides an easily accessed set of decision-making flowcharts and summary information based on the best available evidence on natural medicine options, including herbs, supplements and dietary advice. Covers 74 common diseases and includes scientifically verified therapies. Softcover, 522 pp. $39.95. #B506



Delmar's Integrative Herb Guide for Nurses by Martha Libster, MS, RN. 2002. Profiles 58 common herbs and conditions they treat. Includes the latest biomedical research and clinical practice information and practical information on how to integrate plant-based therapies into patient care. Extensive cultural information includes folklore and traditional uses. Recommendations for addressing the safe use of herbs in patient care. Softcover, 931 pp. $29.95. #B518

The Desktop Guide to Complementary and Alternative Medicine: an Evidence-Based Approach Ed. by Edzard Ernst, Max Pittler, Clare Stevinson, and Adrian White. 2001. Offers concise information on 64 popular CAM diagnostic methods and treatments; summarizes clinical trial data on the effectiveness of CAM for 38 specific conditions; weighs the benefits and risks of each CAM treatment; and includes a CD-ROM of the book that links to Medline. Softcover, 444 pp. $36.95. #B501



Evidence-Based Herbal Medicine by Michael Rotblatt, MD, and Irwin Ziment, MD. 2002. Analyzes a large quantity of the primary literature on controlled clinical trials and provides reliable and practical information on the uses, pharmacology, efficacy, and adverse effects of approximately 65 herbal medicines and a few non-herbal dietary supplements. Softcover, 464 pp. $29. #B516

NEW EDITION

Herbal Medicine by Rudolf Fritz Weiss, M.D. 2000. 2nd Edition. The now classic text used by M.D.s in Germany. An indispensable modern text in medical herbalism. Many herbs are illustrated. Plant drugs are arranged by clinical diagnoses relating to particular systems. Softcover, 362 pp. $59. #B006 **Classic edition still available.** $49. #B006A

Herbal Medicine: A Concise Overview for Professionals Ed. by Edzard Ernst. 2000. Evidence-based look at herbal medicine that will serve as a useful, fully-referenced guide for physicians, medical herbalists and other healthcare professionals with an interest in plant-based therapy. Addresses regulation in the UK and EU, safety issues, efficacy of herbal drugs, quality and standardization, synergy and more. Softcover, 120 pp. $39.95. #B509

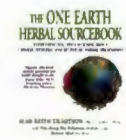
Natural Medicine Comprehensive Database compiled by the editors of Pharmacist's Letter and Prescriber's Letter. 2000. 2nd edition. Contains a listing for almost every natural medicine sold in the U.S. and Canada and a listing for every product discussed in any reputable reference. Information covered includes name of product, also known as, scientific names, uses, safety, effectiveness, possible mechanisms of action and active ingredients, adverse reactions including known allergies, possible interactions, typical dosages and common modes of administration, and other comments. Softcover, 1,310 pp. $92. #B463 Access to web version for 1 year, updated daily. $92. #D008 Both book and web access. $132. #B463C

Principles and Practice of Phytotherapy by Simon Mills and Kerry Bone. 2000. Detailed, practical, and research-based approach to the use of herbal treatments in a wide variety of clinical conditions and problems. Includes a clear description of the principles and foundations for the practice of phytotherapy; in-depth and detailed profiles of over 45 herbs, reviewing pharmacology, research, and traditional use; therapeutics for actual disease states, supported by case histories; and coverage of challenging issues such as dosage, safety, and drug-herb interactions. Fully referenced with more than 4,000 citations. Hardcover, 643 pp. $82.95. #B441

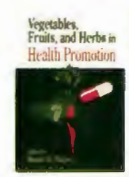
Consumer Education

Jungle Medicine by Connie Grauds. 2001. Story of the author's spiritual journey from being strictly a western pharmacist, through her experiences with an Amazonian shaman, to her rebirth as a shamana who combines her knowledge of western medicine with what she learned in the jungle to form a new spirited medicine. Softcover, 206 pp, $14.95. #B514

Making Plant Medicine by Richo Cech. 2000. The medicine making section includes: drying and processing herbs; making tinctures the easy way; the mathematics of tincturing and solubility factors; basic formulas for fresh and dry extraction, including dosages; vinegar extracts, glycerites, herbal succi and syrups; teas, decoctions, herbal oils, salves and creams; poultices, compresses and soaks; and a section with more than 100 herbs that are readily cultivated in North America. The listings include conservation status, parts used, specific formulas, practical uses, dosages, contraindications and an overview of alternate species. Softcover, 282 pp. $14.95. #B490



The One Earth Herbal Sourcebook: Everything You Need to Know About Chinese, Western, and Ayurvedic Herbal Treatments by Alan Keith Tillotson, Nai-shing Tillotson, and Robert Abel Jr. 2001. Section one provides basic information needed to understand the different types of herb doctors and herbal systems, manufacturing methods, advertising and marketing, and safety and environmental issues. Section two addresses herbal medicines, their components, and how to use them. Reviews 96 herbs, emphasizing the safest and most effective ones. Section three covers herbal protocols for treating some common diseases and strategies for healing via different traditions. Extensive resource guide. Softcover, 596 pp. $20. #B511



Vegetables, Fruits, and Herbs in Health Promotion Ed. by Ronald Watson. 2001. Twenty well-referenced papers that present scientific evidence that increased consumption of vegetables, fruits and herbs improve health. Specific chapters on herbs include "Phytomedicines: Creating

Safer Choices," "Herbal Remedies that Promote Health and Prevent Disease," and "Garlic and Health." Hardcover, 341 pp. $129.95. #B513

General Herbals

Natural Dietary Supplements Pocket Reference by the Institute for Natural Products Research. 2000. Provides thumbnail sketches of more than 30 of the most popular and widely consumed natural dietary supplements in a convenient pocket-sized flipbook. Includes common name, scientific name, botanical family, primary applications, dosage, key active constituents, side effects, drug interactions, cautions, special precautions, and clinical review. Softcover, 96 pp. $14.95. #B493

Legal/Regulatory

Herbs of Commerce Ed. by M. McGuffin, J. Kartesz, A. Leung, and A. Tucker. 2nd edition. 2000. Destined to be the "de facto standard by which all plant common and scientific names will be determined on all products containing herbs" (Christopher Hobbs), this edition lists Latin binomials, Standardized Common Names, Ayurvedic, Chinese (pinyin), and other common names for 2048 species, including 25 fungi and 23 seaweeds. A must-have for anyone who writes about or manufactures herbal products. Hardcover, 421 pp. $95. #B475

Pharmacognosy

Pharmacognosy, Phytochemistry, Medicinal Plants by Jean Bruneton. 2nd edition. 1999. Organized in four parts (primary metabolites, phenols, terpenes and steroids, and alkaloids). Phytochemical generalities, distribution, biosynthesis, extraction and quantization methods, and biological properties. Origin, identity, production, composition, uses, processing, and optimization for each raw material. Therapeutical indication and recommended usage specified for each product. Hardcover, 915 pp. $218. #B149

Research/Technical

Botanical Dietary Supplements: Quality, Safety and Efficacy by Gail Mahady, Harry Fong, and Norman Farnsworth. 2001. Based on a systematic review of the scientific literature from 1975-2000 on some of the top-selling botanicals worldwide. Includes, for each herb, a definition of the crude drug, geographical distribution, a listing of the major chemical constituents, medical uses, pharmacology, contraindications, warnings, precautions, adverse reactions, and dose and dosage forms. Fully referenced. Hardcover, 271 pp. $79.50. #B505

Handbook of Herbs and Spices Ed. by K. V. Peter. 2001. Consists of over 20 chapters covering key spices and herbs, including definition and classification to chemical structure, cultivation and post-harvest processing, uses in food processing, functional properties, regulatory issues, quality indices and methods of analysis. Hardcover, 319 pp. $225. #B508

Medicinal Plants: Culture, Utilization and Phytopharmacology by Thomas S. C. Li. 2000. Presents data for more than 400 species in tables arranged in alphabetical order by Latin binomial. Includes current information on major constituents and medicinal values, toxicity or hazards, essential oil and their fractions, value-added products and their possible uses, cultivation and harvesting, and infectious diseases and insects. Three appendices cross reference major active ingredients and their sources, essential oils and their derivations, and the common and scientific names of the plants cited in the tables. Hardcover, 517 pp. $149.95. #B510

Pharmacodynamic Basis of Herbal Medicine by Manuchair Ebadi. 2002. Demonstrates the beneficial effects and adverse side effects of a large number of herbal drugs, showing their actions and effects on organ, tissue, cellular, and subcellular levels. Includes herbal medications whose pharmacodynamic parameters have been delineated at the molecular level. Discusses the potential interactions of dietary supplements with prescription medications. Hardcover, 726 pp. $129.95. #B517

Quality Control Methods for Medicinal Plant Materials by the World Health Organization. 1998. A collection of recommended test procedures for assessing the identity, purity, and content of medicinal plant materials intended to support development of national standards based on local market conditions. Includes macroscopic and microscopic examination, thin-layer chromatography, and tests for determination of many factors. Softcover,115 pp. $31.50. #B406

Quality Management of Nutraceuticals Ed. By Chi-Tang Ho and Qun Yi Zheng. 2002. 21 symposium papers that examine the chemical and biological quality management of nutraceuticals. Reviews several important classes of compounds, flavonoids, anthocyanins, and marine nutraceuticals. Discusses the chemical analysis of some products on the market such as goldenseal, saw palmetto, green tea, cocoa, and black cohosh. Addresses the bioactivity of several nutraceutical products such as ginger and gum guggal. Hardcover, 327 pp. $135. #B520

The Scientific and Technical Profile of the Genus Thymus by Wudeneh Letchamo, PhD. 2001. Comprehensive and authoritative review of history, botany, taxonomy, chemistry, pharmacology, toxicology, genetics, ecology, cultivation, harvesting, quality control, processing and commerce of the thyme species of the world. Summarizes data from over 700 references. Softcover, 305 pp. $100. #B515

Secretory Structures of Aromatic and Medicinal Plants: a Review and Atlas of Micrographs by Katerina Svoboda and Tomas Svoboda, micrographs by Andrew Syred. 2000. Features 36 light micrographs

and 42 scanning electron micrographs which reveal the anatomy of secretory structures responsible for producing and releasing aromatic components and essential oils of 31 plant species. Extensive bibliography, list of plant species used in aromatherapy, and glossary. Softcover, 60 pp. $45. #B495

Safety/Toxicology

Botanical Safety Handbook: Guide for Safe Use and Labeling for Herbs in Commerce Ed. by M. McGuffin, C. Hobbs, R. Upton, and A. Goldberg. 1997. Provides safety data on more than 550 herbs as guidelines for product labels, including contraindications, side effects, and special warnings. Each herb is classed as can be safely consumed when used appropriately, herbs with the following restrictions, for external use only, or not to be used during pregnancy. Hardcover, 256 pp. $44.95. #B275

Essential Oil Safety by Robert Tisserand and Tony Balacs. 1995. Up-to-date research findings. Practical, comprehensive guide. Detailed profiles of 95 essential oils, including constituents, hazards, dosage, toxicity data and contraindications; brief safety profiles of 311 essential oils and 135 essential oil components; safety guidelines, details of essential oil absorption, metabolism and excretion; oils which may react adversely with certain drugs; and extensive references. Hardcover, 279 pp. $55. #B169

Herb Contraindications and Drug Interactions by Francis Brinker, N.D. 2001, 3rd edition. Information on 240 traditional therapeutic herbs explaining documented contraindications and drug interactions. Appendices identify even more herbs as they affect certain conditions and medicines. Softcover, 432 pp. $25.95 #B282

The Toxicology of Botanical Medicines by Francis Brinker. 2000. 3rd edition. Provides essential information for a basic knowledge of human reactions to certain plant toxins. A concise compilation of traditional knowledge and up-to-date information on the toxic effects of plants and plant extracts that may be used medicinally. Reviews the toxicology of medicinal plants as noted in American pharmacology, pharmacognosy and botanical medicine texts and is updated with recent publication and articles from medical journals. Softcover, 296 pp. $35. #B491

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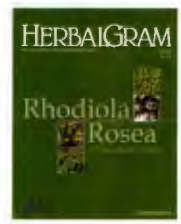

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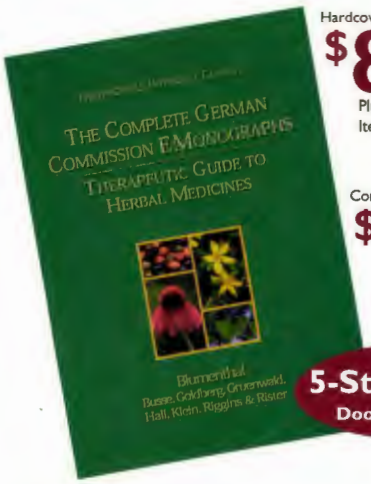

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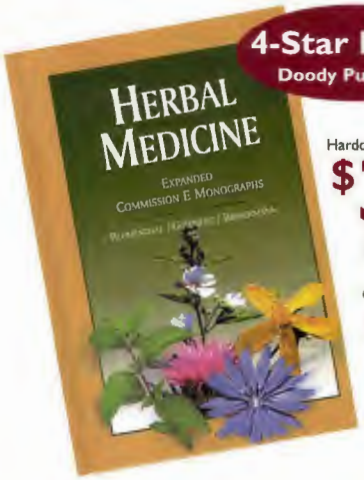

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