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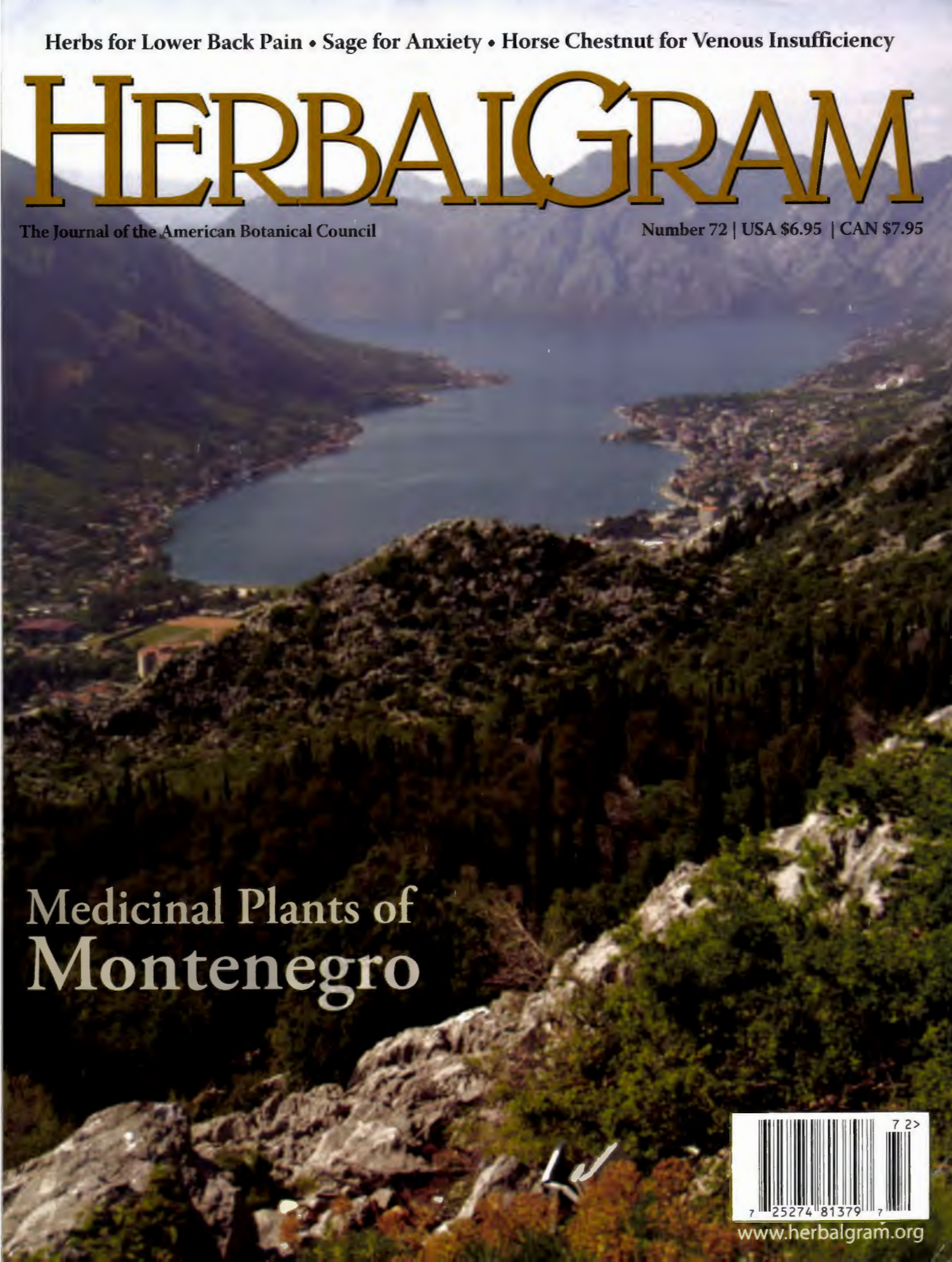

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Peppermint

Mentha x *piperita*

Family: Lamiaceae (Labiatae)

INTRODUCTION

Peppermint is one of the most popular herbs used in today's society.[1] A summer-growing, perennial aromatic herb, peppermint is a hybrid of *Mentha spicata* (spearmint) and *M. aquatica* (watermint). The plant grows wild throughout Europe and North America in moist areas and is thought to be of Mediterranean origin. The leaves and stems of peppermint contain volatile oils that give the plant its pungent fragrance and taste. The oil contains menthol, which is responsible for the sensation of coolness that is characteristic of peppermint.[1]

HISTORY AND CULTURAL SIGNIFICANCE

The genus *Mentha* was named after the Greek nymph Minthe.[2] Legend has it that Minthe was the lover of Pluto, the God of the Greek underworld. When Pluto's wife heard of the affair, she murdered Minthe in a fit of rage and jealousy. In remembrance of Minthe, Pluto brought her back to life as a fragrant plant. The name *peppermint* is from the species name *piperita* meaning "peppery," which distinguishes peppermint from other forms of mint.[2]

The Roman naturalist Pliny the Elder (circa 23-79 CE) wrote that Greeks and Romans used peppermint to adorn themselves and their tables at feasts, and that their cooks used it to flavor both wine and sauces.[3] There is some evidence that *M.* x *piperita* was cultivated by Egyptians, and it appears in 13th century Icelandic medical documents. However, it was not used medicinally in Europe until the mid-18th century.[3]

Peppermint has a long history of unique uses. Aristotle (circa 384-322 BCE) referenced peppermint in his writings as an aphrodisiac.[2] Alexander the Great (356-323 BCE) forbade his soldiers to have peppermint because it was thought to promote erotic thoughts and deplete soldiers of the desire to fight. Arabs used peppermint in their social drinks as a virility stimulant and Romans would spread peppermint on their floors to help get rid of pests.[2]

Peppermint has many modern uses worldwide.[4] Leaf preparations are made from either fresh or dried leaves, while the oil is distilled from freshly-harvested sprigs.[4] Many believe that peppermint is too intense for subtle dishes, but leaves or their essential oil are commonly found in tea, chocolate, confections, chewing gum, jellies, and sauces.[5] Peppermint can also be added to chilled soups or rice on warm days to help cool down the body.[5]

In traditional herbal medicine peppermint has reportedly been used as a tonic for preventing gas, relieving spasms, and other stomach ailments.[3,6] Its traditional use also includes treatment of cholera and diarrhea, to raise body heat and induce perspiration, to treat colds, flu, hysteria and nervous disorders,[3] as well as to assist in alleviating tension headaches.[4] Today, the peppermint plant is commonly added to cough and cold remedies because of its high menthol content, which provides a sensation of coolness and easier breathing.[7]

The tobacco industry uses peppermint oil largely as a flavoring and for its high concentration of menthol and cooling sensation in filtered cigarettes, cigars, and both chewing and pipe tobacco.[6] Due to its unique fragrance, peppermint is often found in soaps, detergents, creams, lotions, and perfumes.[6]

MODERN RESEARCH

Studies have been conducted to evaluate peppermint's documented and potential effects on various gastrointestinal and neurological conditions such as dyspepsia[8,9,10,11] and tension headaches (oil used topically).[12,13] Peppermint's antispasmodic and antidiarrheal effects are topics of continued research.[14] Enteric-coated peppermint oil capsules have been shown to be effective in clinical trials for treating irritable bowel syndrome[15,16,17,18,19,20,21] and the oil has been used effectively to reduce fecal odor in cholostomy bags[22] and to reduce colonic spasms during barium enema[23,24] and colonoscopy.[25,26]

FUTURE OUTLOOK

The world production of peppermint is more than 4000 tons per year with the United States accounting for over 90% of the production.[27] There has been a steady increase in demand for peppermint because of its many uses and because of recent expansion into the Asian market. The plant requires certain environmental conditions that greatly limit suitable areas for cultivation. Because of the high demand and climatic constraints, it is becoming common for peppermint crops to be harvested twice each season (double harvesting) in the United States. Double harvesting can lead to rootstock depletion and can diminish the quality of oil produced. Horticulturists have also encountered a growing pest infestation that is leading to excessive leaf loss and consequently lower oil quality.[27] HG

—Gayle Engels, Meredith Podraza, and Adrian Sierant

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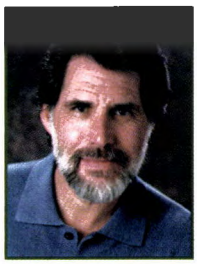
Black Cohosh Safety



Do black cohosh preparations require a warning for possible liver toxicity? Yes, according to some regulators, and no, according to many herb experts. The popular herb used for menopausal symptoms is under increased scrutiny. We reported in our last issue that Australian health authorities issued a required label warning in February. Then agencies in the EU and UK issued label warnings in July. In August, Health Canada released a consumer advisory but did not go so far as to require a label warning. They acknowledged that there is simply inadequate data to prove a causal link between the use of black cohosh and the reported liver toxicity cases, many of which were poorly documented. The identity of the herbal material in most implicated preparations lacked adequate confirmation, a persistent problem with such reports.

In September a lawsuit against two dietary supplement manufacturers, whose products were implicated by a patient who received a liver transplant in Nebraska, was dismissed by the presiding judge who stated that the plaintiff's case and the testimony of her scientific experts failed to meet the test for adequate scientific merit. This is reasonable, as no published scientific evidence to date shows any confirmed molecular or mechanistic basis for suspecting black cohosh rhizome or its extracts as being hepatotoxic, nor any hint thereof. Human clinical trials in which the levels of liver enzymes have been monitored reveal no basis for suspected hepatotoxicity.

As reported in our last issue, the US National Institutes of Health (NIH) conducted a one-day workshop in November 2004 on the safety of black cohosh, concluding that there was inadequate evidence to suggest a causal link to the reported cases of liver toxicity, but also requiring that all NIH-funded clinical trials begin to monitor liver enzymes (elevated liver enzymes are an indicator of liver dysfunction).

At least two reasons can be offered to explain the *appearance* of a potential problem. One is that in any population of humans, there will be unexplainable cases of spontaneous liver toxicity. One study of adults in a Canadian health care system concluded that there are 24 such cases per every 100,000 patients, with the etiology of these cases being unrelated to any detectable organic dysfunction, hepatotoxic drugs, etc.

Another potential explanation is the possibility that the "black cohosh" in some of the implicated products may have been another herb, or possibly a different species of black cohosh. A recently published study analyzed 11 "black cohosh" preparations sold in the United States and found that 3 of the products contained different species of *Actaea* (*A. cimicifuga*, *A. dahurica*, and *A. yunnanensis*) but not the proper species (*A. racemosa*, syn. *Cimicifuga racemosa*) required by US industry trade policy and FDA regulation for the name "black cohosh." Whether these other species of *Actaea* might contain some hepatotoxic compounds or not remains unclear at this time.

Nevertheless, the evidence thus far strongly supports the overall safety of properly manufactured herbal preparations containing black cohosh. The world-renowned Professor Norman R. Farnsworth of the University of Illinois at Chicago, a founder and trustee of ABC and the principle investigator of an NIH-funded clinical trial on black cohosh, has said that insufficient scientific and clinical evidence currently exist to confirm the alleged hepatotoxicity of black cohosh, and any regulatory policy suggesting required warnings is premature and "not rational." Numerous other experts agree.

Nevertheless, some companies have begun to consider adding warnings on black cohosh preparations, not because the currently available evidence warrants such action, but because they are concerned about product liability exposure. Ironically, the presence of such warnings on herb products may reduce consumer usage—an unfortunate development considering that black cohosh is one of the safest and probably the most effective alternative treatments to conventional hormone therapy for menopausal symptoms. HG

Mark Blumenthal

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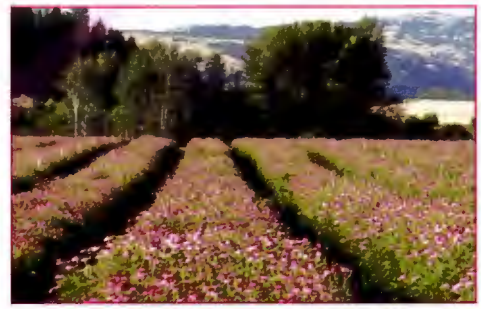

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HERBALGRAM

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features

Wild pomegranate *Punica granatum*. Photo ©2006 stevenfoster.com

departments

On the Cover

Overlooking the medieval city of Kotor, a UNESCO World Heritage Site on the Bay of Kotor, whose mountains along the Adriatic coast harbor Mediterranean herbs such as myrtle (*Myrtus communis*), juniper (*Juniperus communis*), and sage (*Salvia officinalis*). Photo ©2006 stevenfoster.com

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ABC Adds Two New Members to Advisory Board

by Nancy Moon

In a June 2006 press release, the American Botanical Council announced the appointment of new members to its Advisory Board: John A. Beutler, PhD, and John H. Cardellina, PhD.

Dr. Beutler is a well-known pharmacognosist (one who studies drugs of natural origin) and Dr. Cardellina is a highly regarded natural products chemist. Both scientists are employed as researchers at the National Cancer Institute (NCI), a division of the US Department of Health and Human Services' National Institutes of Health (NIH).

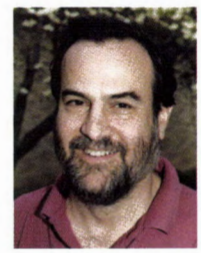
"We are deeply grateful and honored to have these two respected, world-class scientific researchers become formally associated with ABC," said ABC's Founder and Executive Director Mark Blumenthal. "We have enjoyed many years of cooperation with and support from each of these outstanding gentlemen and we thought it was past time for us to publicly acknowledge their contributions to ABC's nonprofit educational mission."

John A. Beutler is a Staff Scientist in the Molecular Targets Development Program at the NCI in Frederick, MD. Dr. Beutler received his doctorate in pharmacognosy from Professor Ara Der Marderosian at the Philadelphia College of Pharmacy and Science (now known as University of the Sciences). He has extensive expertise in the study of plant-derived anti-tumor agents. Dr. Beutler is currently the co-editor-in-chief of *Review of Natural Products* and was formerly the editor of the *Quarterly Journal of Crude Drug Research,* now published as *Pharmaceutical Biology.*

Beutler

"It's a pleasure to formalize the long-standing relationship I have had with *HerbalGram* and ABC," said Beurler. "The work of ABC is really important for public health, both in highlighting useful herbs, and pointing out potentially risky ones."

John H. Cardellina is the Expert Chemist at the Developmental Therapeutics Program at NCI in Frederick. Dr. Cardellina was formerly the vice-president for botanical sciences at the Council for Responsible Nutrition in Washington, DC, a leading dietary supplement industry trade association, and he is also the past-president of the American Society of Pharmacognosy, a professional organization of research scientists. In addition to his research at NCI, Dr. Cardellina serves as a book reviewer for both *Journal of Natural Products* and *Journal of the American Chemical Society.*



Cardellina

"I am delighted and honored to be part of the ABC team, in some small way," said Cardellina. "I've always appreciated the effort and commitment of ABC to provide accurate, timely, and useful information on botanicals and products made from botanicals."

In addition to numerous other duties, the primary role Advisory Board members play at ABC is participating in the peer review of ABC publications. They also assist in an advisory capacity, helping to determine ABC policy and activities. Drs. Beutler and Cardellina join 64 other scientists, clinicians, and other experts who currently comprise the ABC Advisory Board. The names of all 66 ABC Advisory Board members are listed in ABC's quarterly peer-reviewed journal, *HerbalGram*, and on the ABC Web site (www.herbalgram.org). HG

ABC Medicinal Tree Garden

Trees have provided humankind with medicines since ancient times. It has long been part of the ABC garden plan to develop a "Medicinal Tree Walk" along the south edge of the Case Mill Homestead property at ABC Headquarters.

The first trees planted in the young tree garden were a couple of ginkgos (*Ginkgo biloba* L., Ginkgoaceae) and hawthorns (*Crataegus monogyna* Jacq. and *C. laevigata* [Poir.] DC, Rosaceae) that were relocated from other gardens. A year or two later, garden staff planted black walnut (*Juglans nigra* L., Juglandaceae), thuja (*Thuja occidentalis* L., Cupressaceae), cascara sagrada (*Frangula purshiana* [DC] J.G. Cooper, Rhamnaceae), smooth sumac (*Rhus glabra* L., Anacardiaceae), and hydrangea (*Hydrangea arborescens* L., Hydrangeaceae). This year, a few more trees were added, including tea tree (*Melaleuca alternifolia* [Maiden & Betche] Cheel, Myrtaceae), bay (*Laurus nobilis* L., Lauraceae), southern magnolia (*Magnolia grandiflora* L., Magnoliaceae), and two species of eucalyptus (*Eucalyptus globulus* Labill. and *E. melliodora* A. Cunn. ex Schauer, Myrtaceae).

ABC received a few trees and shrubs too late to plant this year. They were planted in larger pots and are being tended until they can be planted this fall. They include slippery elm (*Ulmus rubra* Muhl., Ulmaceae), purple willow (*Salix purpurea* L., Salicaceae), and witch hazel (*Hamamelis virginiana* L., Hamamelidaceae).

Because ABC wants a wide variety of medicinal trees on the property, the garden staff occasionally plants a tree from a different geographical area not really knowing whether it will do well in Central Texas or not. Thus far, the trees that ABC has lost and is fairly certain won't grow in Austin include horse chestnut (*Aesculus hippocastanum* L., Hippocastanaceae) and sea buckthorn (*Hippophae rhamnoides* L., Eleagnaceae).

There are still a number of trees that ABC staff desires for its flourishing medicinal tree garden. Among them are pomegranate (*Punica granatum* L., Punicaceae), mimosa (*Albizia julibrissin* Durazz., Fabaceae), buckthorn (*Rhamnus cathartica* L., Rhamnaceae), and a variety of fruit-bearing trees. The best time to plant a tree may have been 20 years ago, but the next best time is now. In a few years, it will be time to lay the path that will allow staff and visitors to ramble among the medicinal trees and learn about their benefits to human health. HG

—Gayle Engels

ABC Announces Major Redesign and Upgrades to Web Site

ABC's content-rich Web site—www.herbalgram.org—will soon be easier to navigate and will offer you more of the information you want about the traditional uses and modern science behind medicinal plants.

Whether you are a healthcare practitioner, student or professor, herbalist, scientist, or employee in the natural products industry, you can now register your preferences with ABC when you visit the Web site and receive customized e-mail updates on the information you want, such as research reviews, feature articles from our quarterly journal *HerbalGram*, herb profiles and monographs, clinical updates, upcoming events, the latest media coverage on herbal topics, and more.

ABC members will continue to receive access to protected areas of ABC's site through a secure username and password, and the online membership and shopping transactions are still secure and easier to use than in the past.

To upgrade the Web site and improve communications with you, ABC has partnered with Convio—an Internet software and services company assisting non-profit organizations with their online presence and with electronic communications to their members and supporters. Conveniently based near ABC's headquarters in Austin, Texas, Convio works with more than 600 other non-profit organizations around the world. The privately-held company was founded in 1999 and has shown dramatic growth during the past 7 years.

ABC chose Convio because of its proven track record and the benefits this partnership will bring to ABC and its members and stakeholders. With Convio's help, ABC can better serve you through electronic communications, and can also devote more in-house educational resources to fulfilling ABC's nonprofit mission—educating people about the traditional and scientific information that supports the responsible use of herbal medicine. HG

—Aileen Truax

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ABC Employee Profile: Cassandra Johnson

Because nonprofit organizations are typically under-funded, employees of nonprofits must be trained to perform numerous and varied tasks, many of which are not always in the same domain of activity. ABC is no exception.

Cassandra Johnson is someone who wears lots of different hats and covers many bases here at ABC, all of which are essential to the organization's daily operations. She initially started working in various administrative and editorial areas. Her responsibilities in those capacities have included editing *HerbClips*, working with the Development Department, and acting as receptionist—all at the same time. With a journalism degree from the University of Texas, her work for ABC has continued to gravitate towards editorial programs. Over the past year, Cassandra has acted as the managing editor of HerbalEGram, ABC's monthly electronic newsletter for all ABC members.

Johnson

Cassandra also is involved in maintenance of the ever-growing ABC Web site. This includes posting the new *FasTraks HerbClips* and *HerbClip News* to the Web site twice monthly. She edits the Web site in response to requests from staff, which includes updating the home page, correcting any typos, posting press releases, and posting new items to the ABC conference and event calendar. She is also in charge of maintaining statistics on Web site traffic and usage.

Her other varied tasks include helping to fulfill requests from ABC members and ensuring that they receive their many benefits. She also performs editing work for the Education Department. Recently, she was assigned the task of managing book reviews for *HerbalGram.*

As if all this were not enough, Cassandra also assists the Development Department in many ways, including preparing new member and renewed member acknowledgement packets for mailing and maintaining donor records for the Combined Federal Campaign, a program through which federal employees can identify nonprofit organizations for donations via payroll deductions. And she performs numerous other development-related tasks. All these duties are handled by Cassandra reliably and efficiently, with no complaints as to her heavy workload.

The bottom line is that Cassandra Johnson performs many different functions for ABC that cross a wide spectrum of activities, helping to ensure that ABC continues to grow and function properly while providing its many members with increasing benefits. HG

—Mark Blumenthal

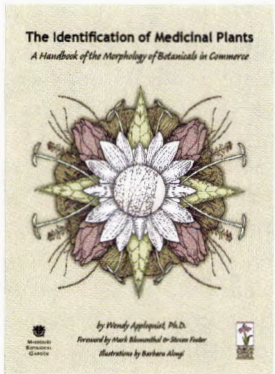
ABC Publishes Crucial Quality Control Manual for Accurate Identification of Herbs and Herbal Products

The occasional misidentification of herbs can result in improper use and potential safety issues. As part of its educational mission to promote responsible use of medicinal plants the American Botanical Council (ABC) proudly announces its newest publication, a crucial quality control manual for herb and dietary supplement companies. *The Identification of Medicinal Plants: A Handbook of the Morphology of Botanicals in Commerce* focuses on the straightforward visual, macroscopic (examination under hand lens or dissecting microscope) identification of more than 150 species of botanicals used in commercial herbal products in North America.

Written by Wendy Applequist, PhD, a botanist at the Missouri Botanical Garden (MBG), the handbook is intended to provide widespread access to the information required for the accurate identification of medicinal plants. This will ensure availability to a wider group of quality control and laboratory technicians in the herb and dietary supplement industry, as well as botanists, medicinal plant collectors, researchers, students, and others.

"As an independent science-based educational organization, ABC is committed to helping make available resources that promote the highest quality herb and botanical preparations," said Mark Blumenthal, founder and executive director of ABC. "Proper identity is the initial requirement for herbal quality, and this book will become a standard reference for all in the herb industry to help ensure optimum quality control for the greatest benefit to consumers."

The handbook features 113 botanical entries covering more than 150 different species of botanicals in commerce, plus 87 detailed black-and-white line drawings. It also contains a brief review of basic plant structure, some practical advice on identification, an introduction to botanical nomenclature, a glossary, a reference list, and an index.



The first step in quality control of botanical preparations is ensuring the correct identification of the plant material intended for use. Detailed descriptions by Dr. Applequist, assistant curator at MBG, plus drawings by Barbara Alongi provide excellent guidance for properly, effectively, and efficiently identifying botanicals.

The book has already received accolades from numerous herbal experts in a variety of fields including academia, pharmacology, and numerous others, particularly those with experience in botanical identification in setting quality standards in the herb industry. James A. Duke, PhD, internationally noted herbal expert and author, said the new handbook is a "great book" containing "good science" and "good art" and that it is "very useful."

"As a collector of books and articles on powder analysis and the nomenclature of medicinal plants, this book is a good accompaniment that pulls together information from a wide number of sources. Great job and a great addition to my bookshelf!" said Arthur O. Tucker, PhD, research professor and co-director of the Claude E. Phillips Herbarium at Delaware State University.

Josef A. Brinckmann, vice-president of research and development at Traditional Medicinals, a leading marketer of medicinal herbal teas, stated, "The botanical glossary, the detailed macroscopic descriptions including sensory characteristics, and the illustrations will make this an often-used handbook sitting alongside the pharmacopeias and other essential laboratory handbooks."

Sidney Sudberg, a chiropractor and acupuncturist who now is director of Alkemists Pharamaceuticals, Inc., a third-party quality control and consulting laboratory for the herb industry said, "This book is indispensable to anyone who loves plants, and herbs in particular, and wants to know that they have the correct species. As a quality control professional interested in having as complete a picture as possible for accurate identification of herbs, this book is a necessity."

Passionflower ***Passiflora incarnata*** by Barbara Alongi from *The Identification of Medicinal Plants: A Handbook of the Morphology of Botanicals in Commerce* by Wendy Applequist.

The book retails for $89.95, with a discount for ABC members. ABC is currently taking advance orders and will begin shipping orders in October. To order now, call 800-373-7105 and request item #B539. HG

—Tara Hall

Book Data

The Identification of Medicinal Plants: A Handbook of the Morphology of Botanicals in Commerce by Wendy Applequist. Austin, TX: American Botanical Council; 2006. Item #B539; Hardcover; 231 pp.; 87 B&W line drawings; $89.95. ISBN 10: 0-9655555-1-8; ISBN 13: 978-0-9655555-1-7

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Journal of Natural Products Dedicates Special Issue to Farnsworth

by Courtney Cavaliere

A special issue of the *Journal of Natural Products* (JNP) was published in March 2006 in honor of Norman R. Farnsworth, PhD, research professor of pharmacognosy and distinguished university professor at the University of Illinois at Chicago. Among his numerous positions, consultancies, and activities, Dr. Farnsworth is also a founding member of ABC's Board of Trustees.

The special JNP issue featured an editorial documenting Dr. Farnsworth's contributions to pharmacognosy and natural products research, including his many research and academic achievements, his service on various expert committees and panels, and his establishment of the NAPRALERT database.[1] According to the editorial, co-written by long-time Farnsworth colleagues Harry H.S. Fong, PhD, Geoffrey A. Cordell, PhD, and A. Douglas Kinghorn, PhD, "Professor Farnsworth is the quintessential renaissance man, who along with such distinguished colleagues as Arthur E. Schwarting, Varro E. Tyler, and Jack L. Beal, among others, almost half a century ago, helped transform pharmacognosy from descriptive medical botany and mycology into the dynamic chemistry- and biology-based multidisciplinary science that it is today." The journal issue further recognized Dr. Farnsworth through its selection of articles, all of which were chosen to reflect Dr. Farnsworth's broad scientific interests.

Norman Farnsworth, PhD, speaks at ABC's American Botanical Celebration in January 2006. Photo ©2006 stevenfoster.com

Contributors to this special edition included Fredi Kronenberg, PhD, Edward J. Kennelly, PhD, Gordon M. Cragg, PhD, Mahabir P. Gupta, PhD, Michael Heinrich, PhD, John M. Pezzuto, PhD, Elaine Elisabetsky, PhD, D. Doel Soejarto, PhD, Barbara N. Timmermann, PhD, Ikhlas A. Khan, PhD, Arnold Vlietinck, PhD, David G.I. Kingston, PhD, Lars Bohlin, PhD, Tom J. Mabry, PhD, Connie M. Weaver, PhD, V. Srini Srinivasan, PhD, Gabriel I. Giancaspro, PhD, David B. Roll, PhD, Jennifer Salguero, RPh, John P.N. Rosazza, PhD, and John M. Cassady, PhD.

The *Journal of Natural Products* is a publication of the American Chemical Society (ACS) and the American Society of Pharmacognosy (ASP). (It was originally called *Lloydia,* in honor of the famous medicinal plant researcher John Uri Lloyd, and was initially published as the official journal of ASP.) Dr. Farnsworth was a founding member of ASP, and he is the organization's only founding member still actively engaged in academia and conducting natural product drug discovery and botanical dietary supplement research.[1] The issue honoring Dr. Farnsworth is the third of the journal's 69th volume. It is available for purchase through ACS (http://pubs.acs.org/journals/jnprdf/media/order_info.html). The Table of Contents and the editorial described above are accessible online, free of charge, at http://pubs.acs.org/cgi-bin/sample.cgi/jnprdf/2006/69/i03/html/np068000l.html.

Several articles in recent *HerbalGram* issues have featured Dr. Farnsworth's latest awards and accomplishments.[2,3,4] An article in the May 2006 issue of HerbalEGram and the 71st issue of *HerbalGram*, "NAPRALERT Herbal Database Available on Internet," provides an update on the increased accessibility of NAPRALERT, the world's largest database on medicinal plant research, established by Dr. Farnsworth and his colleagues in 1975.[5] HG

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NNFA Becomes NPA, Opens New Offices

by Madeline Hollern

The summer agenda of the National Nutritional Foods Association (NNFA) annual convention went beyond celebrating the organization's 70th anniversary this year. Within 6 weeks of June and July of 2006, NNFA, the national trade association for the health and natural products industry, accomplished the following major achievements: changed its company name to the Natural Products Association (NPA); moved its headquarters to Washington, DC; opened a branch office in Beijing, China; and expanded its product testing program for supplements for athletes.

Name Change

NNFA announced its name change during its 70th anniversary celebration on July 15, 2006.[1] Members of the association voted on the new name, which passed with a large majority. The name is intended to "more accurately describe the organization's diverse membership and position the association to keep pace with the dynamic natural products marketplace," according to an NPA press release.

"Our new name not only reflects the breadth of our existing membership, but it also recognizes the association's position as the overarching trade organization for the natural products industry," said NPA President David Taylor.[1] "Along with our recently adopted mission and vision statements, our name change will allow us to emphasize that we really are the 'big tent' organization for retailers and suppliers of natural products."

NPA launched a comprehensive re-branding effort for the summer and fall to promote the new name and reconnect with stakeholders and consumers of natural products. Since its founding in 1936, the organization has changed names 4 times. After its first year as the American Health Food Association, the title changed to the Natural Health Foods Association. In 1943 the organization changed its name again to the National Dietary Foods Association, and in the 1980s it switched to the National Nutritional Foods Association.

Headquarter Shift

On June 1, 2006, NPA (then NNFA) opened its Washington, DC headquarters. According to a company press release, the new location, in the Dupont circle of Washington, is intended to foster continued growth of the organization, its advocacy efforts, and its representation for the natural products industry.[2]

"We are extremely proud," said NPA President David Taylor.[2] "We see this move as a tremendous investment for our membership, and a symbol of our ongoing commitment to effective Washington representation for the natural products industry."

The association's new address is 1773 T St., NW, Washington, DC, 20009.

New China Office

In July, NPA announced the opening of a new branch office in Beijing. The building will establish a physical presence for NPA in China, where dietary supplement sales are expected to grow to more than $10 billion within the next few years.[3]

"The Natural Products Association has long recognized that strong international presence is beneficial for our membership and the industry," said Randy Dennin, chairman of the Natural Products Association China.[3] "We are committed to facilitating trade among nations and have a strong stake in maintaining high standards for product quality, both domestically and internationally."

The new office will work closely with NPA in the United States in organizing annual trade missions and will act as a liaison to visiting dietary supplement companies looking for business transactions in China. The office is not the first overseas venture of the company; in 1998 NNFA Japan was established. Both ventures aim to obtain consumer and industry-friendly regulations.

"It's great to see the Natural Products Association's China initiative reach this milestone," said NPA Executive Director and CEO David Seckman.[3] "Experience has demonstrated that the combination of a trusted in-country contact who is both familiar with the local marketplace and has established relationships with key officials are imperative to entering and thriving in China."

Product Testing Expansion

To assure customers that sports supplements do not contain traces of banned steroidal and stimulant ingredients, NPA is expanding its TruLabel random testing program.[4] Plans for the expansion were announced July 15, 2006, in response to raised concerns among athletes and sports organizations.

"The notion that dietary supplements contain unlisted ingredients that are responsible for positive steroid and other banned substance tests is simply wrong," said Daniel Fabricant, PhD, vice president of scientific affairs for the NPA.[4] "By testing products through our TruLabel program we're looking to provide sound evidence that our member manufacturers are committed to providing quality and uncompromised results for their customers."

NPA's TruLabel has operated since 1990 and is one of the dietary supplement industry's oldest self-regulatory programs. In addition to TruLabel, NPA has had a companion self-regulatory effort for the past 7 years with a third-party certification program, which also strives to ensure quality throughout the manufacturing process.

NPA membership is comprised of more than 9,600 retailers, manufacturers, wholesalers, and distributors of natural products, including foods, dietary supplements, and health and beauty aids.[2] More information on NPA is available at its Web site, http://www.naturalproductsassoc.org. HG

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Panel Explores Safety of Soy on Reproduction and Fetal or Infant Development

by Courtney Cavaliere

A panel of 14 independent experts convened by the US Center for the Evaluation of Risks to Human Reproduction (CERHR) and the National Toxicology Program (NTP) determined that the phytoestrogen genistein found in soybeans does not pose a reasonable threat to human reproduction and development, based on available data. The panel noted that insufficient data exists, however, to permit a determination of the safety of soy infant formula.[1]

During a 3-day meeting, held March 15-17, 2006, in Alexandria, VA, the panel reviewed studies of laboratory animals and humans to determine whether genistein or soy formula might cause adverse effects on human reproduction and/or development of a fetus or infant. The panel ultimately expressed negligible concern for reproductive and developmental effects from exposure of adults, who they claim are unlikely to consume daily levels of genistein sufficient to cause adverse effects in such areas. The panel members further expressed negligible concern for adverse effects in neonates and infants who consume up to 0.01-0.08 mg/kg body weight/day of genistein (the aglycone form of genistin) contained in soy formula. Of the total amount of genistein/genistin in soy formula only about 1% is present in the uncomplexed aglycone form. With respect to soy formula's overall reproductive or developmental toxicity, the panel argued that poor study designs, insufficient sample sizes, and otherwise insufficient data of case-studies and trials prevented its members from arriving at a clear determination of safety.

The full genistein and soy formula expert panel reports are available at the CERHR Web site, at http://cerhr.niehs.nih.gov/. CERHR and NTP are jointly preparing monographs of genistein and soy formula based on the panel's findings and on public comments submitted to CERHR by July 5. The monographs will be available to the public on the CERHR Web site and distributed to appropriate federal health and regulating agencies.

A recent editorial by Kenneth D.R. Setchell, PhD, professor of pediatrics at the University of Cincinnati College of Medicine, addressed the panel's findings.[2] According to Dr. Setchell, soy formula's 40-year history of use with little documentation of adverse effects attests to its safety. He further pointed out that animal testing does not adequately demonstrate the potential effects of soy or genistein on human infants, signaling a need for prospective studies of risks and benefits of soy, in place of further animal trials. According to an article in *Environmental Health Perspectives*, the world's largest longitudinal study of children and their consumption of soy-based formula, cow's milk-based formula, and breast-milk is currently underway, under the direction of Thomas Badger, PhD, of the Arkansas Children's Nutrition Center.[3]

It is estimated that 20-25% of infants in the United States consume soy infant formula at some point during their development.[3,4] Soy food sales reached nearly $4 billion in the United States in 2003 and are expected to continue to rise, according to the Soyfoods Association of North America.[5] HG

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Moroccan Argan Trees Threatened by Climbing Goats

by Madeline Hollern

When the drought-ridden meadows of Morocco fail to satiate its native goats, the land-based animals look upwards for sources of sustenance—way up to the branches of the Argan tree. The trees' water-filled leaves and olive-like fruit often tempt the goats into climbing the thorny evergreens. In an unorthodox spectacle, the goats hoist themselves up the trees' twisted trunks, perch atop the branches like birds, and ingest the trees' fruit and water.[1]

Argans (*Argania spinosa* L., Sapotaceae) have been enticing goats for centuries. The tree is a relic species of the Tertiary Period (which took place about 65 to 1.6 million years ago).[2] Throughout history, the goats' gravity-defying behavior has indirectly provided a service to Moroccan locals. After eating the Argan fruit whole, goats spit up or excrete its pits, much to the delight of Berber farmers, who gather the pits for industrial purposes. Undigested argan pits can be split to extract bitter internal kernels, which farmers grind and press to make nutty oils used for cooking or cosmetics. But the tree's profitable possibilities go beyond these oils, as Argans have also traditionally been used for purposes ranging from timber, firewood, and charcoal to ornaments, soap, and medicine.[3]

Photo ©2006 Fouad Zahiri

Argan trees, also known as Moroccan ironwoods,[3] grow primarily between Essaouira and Agadir in Southwest Morocco.[1] They can survive heat, drought, and poor soil, making them suitably adapted for harsh African environments. The trees grow up to 10 meters high and typically live up to 200 years.[2] But despite the adaptability of Argan trees, current overgrazing by goats and commercial overuse of its wood has reduced the number of surviving trees to 50% of what it was 50 years ago, making its future uncertain.

Although locals often refer to the Argan tree as "The Tree of Life," their poor treatment of the tree's environment has largely contributed to its steady demise.[3] Increasing amounts of people with large domesticated grazing herds continue to move into the area, resulting in overgrazing of the fragile ecosystem. Even worse, the tree has never been germinated from seed or transplanted from cuttings on a wide scale.[2] Unsustainable collections of firewood, timber, and fruit have also caused a sharp decline in the tree's population, as has the abandonment of traditional land management in favor of more modern agricultural practices like plowing and irrigated crops. Global warming and the disappearance of spiny "nurse" plants such as *Rhus pentaphylla* Jacq., Anacardiaceae and *Ziziphus* spp., Rhamnaceae, which protected Argan tree seedlings, could also be culprits.[3]

To combat the demise of the Argan tree, several entities have created an alliance to raise awareness of its inherent value. Groups like UNESCO, Prince Albert II of Monaco, and Cooperative Amal, the country's first oil cooperative, are discouraging locals from chopping down the tree for firewood and encouraging more careful goat grazing.[2] UNESCO has declared a 10,000-square-mile patch of land between the Atlantic and the Atlas Mountains as a "biosphere reserve," providing money to manage the preservation of the trees. To halt overgrazing, Cooperative Amal led a campaign to ban grazing in the trees from May to August, when the fruit ripens and eventually falls to the ground. So far the ban has left enough fruit on the ground to supply the growing number of oil cooperatives while still protecting the trees.[2]

The alliance has also created a global market for Argan oil, which is one of the rarest and most expensive oils in the world.[3] Monaco's Prince Albert II has sponsored cooperatives to encourage the oil's export, while worldwide chefs and society matrons are praising the culinary qualities of the oil and its anti-aging effect on skin.[2] To make Argan oil, each nut has to be cracked open to remove the kernels, so making one liter of oil can take up to 20 hours of work.[1] The edible hazelnut-like oil is used in a Berber breakfast condiment called *amlou* while the cosmetic oil, rich in vitamin E and essential fatty acids, is used for massage, facials, aftershave lotion for men, hair conditioning, and nail fortifying.[2,4] The oil sells for over $25 for an 8.45 oz bottle in some European and American gourmet food shops.[2,5]

By increasing the economy and providing jobs to locals, the Argan tree remains a necessary economic asset to Moroccans, who in turn fight to keep their "Tree of Life" alive and thriving. HG

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Reviewed: Engelman U, Walther C, Bondarenko B, et al. Efficacy and safety of a combination of Sabal and Urtica extract in lower urinary tract symptoms. *Arzneim-Forschung/Drug Res.* **2006;56(3):222-229.**

More than 60% of males in the second half of life show evidence of benign prostatic hyperplasia (BPH), i.e., based on clinical observations of urinary symptoms and/or on histological examination. BPH may result in obstruction and irritation of the lower urinary tract with symptoms such as incomplete voiding, nighttime urination, and decreased urinary flow.

Two types of conventional pharmaceutical drugs have demonstrated efficacy in the treatment of these lower urinary tract symptoms (LUTS), although the etiology of BPH has not been fully elucidated. The 5-alpha-reductase inhibitors, such as finasteride (Proscar®, Merck), block the conversion of testosterone to dihydrotestosterone, which is believed to be responsible for some of the swelling of the prostate. The selective alpha$_1$-adrenoceptor antagonists block post-synaptic alpha$_1$-adrenergic receptors, resulting in relaxation of smooth muscle in the bladder neck and prostatic urethra. Drugs that act selectively on specific alpha-$_1$ subtypes cause fewer unwanted side effects (e.g., sexual dysfunction) than 5-AR inhibitors.

In placebo-controlled studies, the selective alpha$_{1A}$-adrenoreceptor antagonist tamsulosin (Flomax®, Boehringer-Ingelheim), has been shown to effectively reduce subjective LUTS symptoms within 2 weeks of initiating treatment. Improvement in peak urinary flow rate and residual urinary volume reached statistical significance after 4 weeks of treatment and reached maximum benefit after 12-14 weeks.

Plant extracts are also extensively used in many European countries in the management of BPH and they are becoming more popular in the United States. Saw palmetto (*Serenoa repens* [W. Bartram] Small, Arecaceae) fruit (berry) extract and stinging nettle (*Urtica dioica* L., Urticaceae) root extract are the most commonly used herbal preparations in Germany, where 61.6% of men with LUTS are treated with phytomedicines. In randomized, double-blind clinical trials, both of these extracts have demonstrated effectiveness in treating LUTS symptoms. A product that combines both extracts—PRO 160/120 (a fixed combination of 160 mg saw palmetto fruit extract, WS® 1473, and 120 mg stinging nettle root extract, WS® 1031 (both made by Dr. Willmar Schwabe GmbH & Co.)—has been shown in published clinical trials to improve peak urinary flow and improve subjective symptom scores on the International Prostate Symptom Score (IPSS) better than placebo and comparable to the drug finasteride.[1] The IPSS is a self-rating questionnaire regarding lower urinary tract symptoms, including frequency, urgency, nocturia, weak stream, and incomplete emptying.

Saw palmetto *Serenoa repens* Photo ©2006 stevenfoster.com

In the trial being reviewed here, researchers compared the efficacy and tolerability of PRO 160/120 to tamsulosin in patients with LUTS. The study was a prospective, randomized, double-blind, double-dummy, multicenter trial that utilized PRO 160/120. Tamsulosin in 0.4 mg slow-release capsules was purchased from the domestic market. (In a double-dummy design, both treatment groups receive an active treatment as well as a placebo, as explained below.)

The trial enrolled 149 subjects who were recruited from outpatients in 23 private urological practices and outpatient clinics in Germany. Study subjects were suffering from BPH not requiring surgery. Inclusion criteria included age ≥ 50 years, maximum urinary flow rate ≤ 12 ml/s at a urinary volume ≥ 150 ml, and initial IPSS total score ≥ 13. During a 2-week placebo run-in phase, 140 subjects were randomized to receive either 1 capsule 2 times per day of PRO 160/120 plus 1 capsule tamsulosin placebo per day (n = 71) or 1 capsule per day tamsulosin plus 1 capsule 2 times per day of the PRO 160/120 placebo (n = 69). After the baseline examination, follow-up visits were scheduled after weeks 8, 16, 24, 36, 48 and 60 of double-blind treatment. Safety of the treatments was monitored via physical examination, digital-rectal examination of the prostate, and laboratory tests at pre-treatment and after weeks 24 and 60.

Efficacy of treatment was assessed primarily by the change in the IPSS total score between baseline and at the end of the 60th week of treatment. Secondary outcome measures included peak urinary flow rate (measured by an electronic uroflow recorder), average urinary flow rate, urinary output, duration of micturition (urination) and flow increase, and residual urinary volume. The primary analysis, conducted on the intention to treat principle, was based on the full analysis set (FAS)—"all patients who were randomized and received the investigational treatment at least once...." After eliminating patients for protocol violations, the per protocol analysis (PP) was conducted on 78.9% (56 of 71) in the PRO 160/120 group and 78.3% (54 of 69) for the tamsulosin group. The subset of "responders"—patients who had an IPSS total score ≤ 7 at endpoint—was analyzed as well.

The FAS showed that the IPSS score decreased from a median of 20 points at baseline to a median of 11 points in the PRO 160/120 group and a median of 10 points in the tamsulosin group at week 60 (medians with 95% confidence interval). In both the FAS and PP analysis the median intraindividual decrease in the IPSS score was 9 points. The responder rate (IPSS ≤ 7 at endpoint) was 32.4% for PRO 160/120 (22 of 68 patients) and

27.9% for tamsulosin (19 of 68 patients) in the FAS (P = 0.034 for non-inferiority of PRO 160/120). The responder rates in the PP analysis were 32.1% (18 of 56) for PRO 160/120 and 29.6% (18 of 54) for tamsulosin (P = 0.074 for non-inferiority). Both treatments were also comparably effective in a sub-group analysis of patients with a baseline IPSS of ≤ 19 points (moderately severe symptoms) as well as in patients with a baseline score of ≥ 20 points (severe symptoms).

In the LUTS-based Quality of Life assessment (single item, range 0 [very good] to 6 [very bad]), the PRO 160/120 group improved by a median of 2 points, while the tamsulosin group improved by a median of 1 point (FAS, baseline versus treatment end). In the PRO 160/120 group, 36 patients (50.7% of 71), and in the tamsulosin group, 34 patients (49.3% of 69), showed an improvement in quality of life of at least 2 points. The authors write, "With a margin of 13% for non-inferiority of PRO 160/120, treatment with the herbal drug was significantly not inferior to treatment with tamsulosin (P = 0.04)."

Regarding the secondary outcome measures, both groups demonstrated "considerable improvement" in peak and mean urinary flow, and decreased the duration of urination and the amount of residual urine. Neither treatment had an effect on urinary volume, flow increase, prostate size, or sexual functioning.

The researchers concluded that the saw palmetto-nettle root combination phytomedicine was safer than the conventional drug. Fifteen PRO 160/120 patients (21.1% of 71) reported 18 adverse events (AEs) while 19 tamsulosin patients (27.5% of 69) reported 23 adverse events. Researchers assessed these AEs and classified 6 in the PRO 160/120 group and 9 in the tamsulosin group as being drug related. This corresponds to less than 1 AE in 1000 treatment days. The authors therefore rate both drugs as having excellent tolerability "albeit with a 30% advantage regarding AE rates in favor of PRO 160/120."

In conclusion, the authors write that "this study supports the non-inferiority of the [herbal combination] extract PRO 160/120 in comparison to the well investigated and widely used alpha-$_1$-adrenoceptor antagonist tamsulosin" for the amelioration of BPH-associated LUTS. The authors also concluded that "Both drugs reduced the subjective symptoms of BPH to a comparable, clinically relevant extent that had a direct, beneficial influence on the patients' quality of life." This trial should help restore some of the compromised public and professional perception of saw palmetto preparations for treating BPH symptoms that was adversely affected by the publication of a recent trial with a negative outcome, in which a saw palmetto extract did not provide statistically beneficial effects in patients with more advanced (moderate to severe) BPH symptoms.[2] HG

—Cathleen Rapp, ND

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Review of Herbal Medicines to Treat Low Back Pain

Reviewed: Gagnier JJ, VanTulder M, Berman B, Bombardier C. Herbal medicine for low back pain. *Cochrane Database Syst Rev.* April 19, 2006;(2):CD004504.

Back pain is a common condition. In the United States, it is the most common cause of disability in people younger than 45 years.[1] Low back pain is the second most frequent cause of work absence in industrialized nations[2] and is a frequent reason for visits to a physician.[3,4] These authors conducted a review of the scientific literature to determine the effectiveness of herbal medicines compared with placebo, no intervention, or other interventions in the treatment of nonspecific low back pain (defined as "pain between the lowest rib and the bottom of the buttocks that is not caused by serious, underlying problems such as rheumatoid arthritis, infection, fracture, cancer, or sciatica due to a herniated disc or other pressure on nerves").

Included in this review were randomized controlled trials (RCTs) including adults (older than 18 years) suffering from acute (lasting up to 6 weeks), subacute (lasting 6 to 12 weeks), or chronic (lasting longer than 12 weeks) nonspecific low back pain. Herbal medicine was defined as "all or part of a plant that was used for medicinal purposes, administered orally or applied topically." Outcome measures were pain intensity, functional status, overall improvement, and work status.

Devil's claw *Harpagophytum procumbens*
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The authors searched the following databases: Cochrane Complementary Medicine Field Trials Registry (Issue 3, 2005); MEDLINE (1966 to July 2005); EMBASE (1980 to July 2005); and Clinical Evidence (January 2005). In addition, they reviewed reference lists in review articles, guidelines, and retrieved articles, and contacted persons with expertise in herbal medicine and low back pain to identify additional trials. Methodological quality and clinical relevance were assessed separately by 2 of the authors; disagreements were resolved by consensus.

For this review, 10 citations met the inclusion criteria. Three studies used an oral form of the herbal species devil's claw (*Harpagophytum procumbens*, [Burch.] DC. ex Meisn., Pedaliaceae); 3 used an oral white willow bark (*Salix alba* L., Salicaceae); and 4 used topical cayenne (*Capsicum frutescens* L., Solanaceae). Four studies compared various oral herbal medicines with placebo; 2 studies compared oral herbal medicines with standard pain medications; 3 studies compared topical herbal medicines with placebo, and 1 compared a topical herbal medicine with a topical homeopathic medicine.

The authors note that most of the trials reviewed are of moderate or high quality, but they tested only the effects of short-term (up to 6 weeks) use. Also, the authors of half of the studies were judged to have a potential conflict of interest, and 2 others did not discuss conflict of interest.

After conducting the review, the authors of this review conclude that an aqueous devil's claw extract at a standardized daily dosage of 50 mg harpagoside, a white willow bark extract at a standardized dosage of 240 mg salicin per day, and cayenne plaster seem to reduce low back pain more than placebo. "These herbal medicines could be considered as treatment options for acute episodes of chronic low back pain," they write.

Following are the studies reviewed by these authors.

Oral Herbal Medicines Versus Placebo

One 4-week trial tested an extract of devil's claw (Doloteffin®, Ardeypharm GmbH, Herdecke, Germany) standardized to 50 mg harpagoside (H) per day versus placebo in 118 patients with chronic low back pain.[5] Results showed a significant increase in the number of pain-free patients in the 50 mg H group (9% to 17%) over the placebo group (2% to 5%). In another 4-week trial, 197 patients were given either a daily dose of devil's claw extract (WS 1531®, W. Schwabe Pharmaceuticals, Karlsuhe, Germany; standardized to 100 mg H or 50 mg H), or placebo.[6] The number of patients who were pain free for at least 5 days in the fourth week of treatment was significantly higher in the 100 mg group than in either the placebo group or the lower dose (50 mg H) group.

Two studies compared dried white willow bark with placebo. In the first study, 210 patients were divided into 3 groups and given either 2 doses of white willow bark standardized to either 120 mg or 240 mg salicin per day or placebo.[7] The number of patients who were pain free for at least 5 days in the fourth week of treatment increased from baseline in the placebo group (n=4), 120 mg salicin group (n=15), and the 240 mg salicin group (n=27). The authors note that the trend for dose was significant, with the group receiving 240 mg salicin showing more improvement in the pain index than the group receiving 120 mg salicin. A second trial was designed to test platelet aggregation of white willow bark extract (Assalix®, Bionorica, Neumarkt, Germany) but did not measure clinically relevant outcomes.[8]

Oral Herbal Medicines Versus Standard Pain Medication

A study of 88 patients with acute episodes of chronic, nonspecific low back pain were given devil's claw (Doloteffin®) standardized to 60 mg H per day or 12.5 mg rofecoxib (Vioxx®, a nonsteroidal anti-inflammatory drug) per day. Between the 2 groups, no statistically significant differences were seen in the number of patients who were pain free for at least 5 days in the sixth week of treatment.[9]

In a second study, 228 patients were given either a daily dose of willow bark extract (Assalix®), yielding 240 mg salicin, or a daily dose of 12.5 mg of rofecoxib. The study revealed no differences in

effectiveness in the short term for patients with acute episodes of chronic, nonspecific low back pain.[10]

Topical Herbal Medicines Versus Placebo

In one trial, 40 patients with acute mechanical low back pain were treated for 14 days with either a cream called Rado-Salil® (containing ethysalicylate, methylsalicylate, glycosalicylate, salicylic acid, camphor, menthol, and oleoresin capsicum; Will-Pharma; The Netherlands) or a placebo cream containing oils of bergamot (*Citrus bergamia* Risso & Poit., Rutaceae) and oil of lavender (*Lavandula* spp. L., Lamiaceae).[11] An improvement in pain score was seen in the Rado-Salil group, as well as a more favorable rating by both patients and physicians. (It is certainly questionable whether the bergamot and lavender essential oils are inert and thus whether they should have qualified as candidates for use as a placebo.)

In another trial, 154 patients with acute episodes of chronic, nonspecific low back pain were randomly assigned to a placebo plaster group or a group using a capsicum plaster (containing 12 mg of capsaicinoids per plaster) for 3 weeks.[12] A 30% reduction in pain was reported in 60.9% of patients in the capsicum group and 42.1% of those in the placebo group. After treatment, 13.5% of the capsicum group and 6.6% of the placebo group were completely symptom-free.

In another study of patients with chronic low back pain, 320 patients were randomly assigned to a placebo plaster group or a capsicum plaster group for 21 days.[13] (The topical capsicum plaster contained an ethonolic extract of cayenne pepper standardized to 22 mcg/cm^2 of capsaicinoids.) Reduced pain, as well as improved function, was seen in the capsicum plaster group.

Topical Herbal Medicine Versus Homeopathic Treatment

In one trial, 161 patients (mixed group with new acute low back pain and acute episodes of chronic low back pain) were randomly treated for 7 days with either a Spiroflor SRL homeopathic gel (VSM; The Netherlands) or a Cremor Capsici Compositus FNA gel (Ratiopharm; The Netherlands).[14] Each of the gels was applied at 3 g per day. Both groups showed a significant reduction in pain. The authors reported no statistically significant or clinically relevant differences in effectiveness between the 2 gels. Both groups showed a significant reduction in pain on the VAS (Visual Analog Scale), with a decrease of 38.2 mm in the SLR group and 36.6 mm in the CCC group. In the SLR group, 50% of subjects reported that treatment was 80% effective and 18% reported total (100%) effectiveness. In the CCC group, this was 55% and 15%, respectively.

The authors of this review conclude that "An aqueous extract of *Harpagophytum procumbens* at a standardized daily dosage of 50 mg harpagoside, an extract of *Salix alba* at a standardized dosage of 240 mg salicin/day, and a plaster of *Capsicum frutescens* seem to reduce pain more than placebo. These herbal medicines could be considered as treatment options for acute episodes of chronic low-back pain." HG

—Shari Henson
and Courtney Cavaliere

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Sage Leaf Extract Reduces Anxiety in Clinical Trial

Reviewed: Kennedy D, Pace S, Haskell C, Okello E, Milne A, Scholey A. Effects of cholinesterase inhibiting sage (*Salvia officinalis*) on mood, anxiety and performance on a psychological stressor battery. *Neuropsychopharmacol.* 2006;31:845-852.

In human, animal, and in vitro laboratory research, garden sage (*Salvia officinalis* L., Lamiaceae) has been shown to inhibit cholinesterase enzymes, enzymes that break down acetylcholine (Ach), a chief neurotransmitter. Compounds that inhibit acetylcholinesterase (AChE), the specific enzyme that metabolizes Ach, may improve mood in some people by helping to maintain optimal levels of Ach and thus brain activity. Lemon balm (*Melissa officinalis* L., Lamiaceae) also has demonstrated these cholinergic properties and has been shown to significantly reduce the negative mood consequences of a psychological stressor battery.[1,2] The authors of this trial used the lemon balm study as a model to evaluate the anxiety and mood modulating capabilities of sage. This randomized, double-blind, placebo-controlled, crossover study was conducted on 30 healthy volunteers (mean age: 24 years) at the University of Northumbria, Newcastle upon Tyne, UK. Participants received placebo, 300, or 600 mg of dried leaf sage extract (MedicHerb UK Ltd, Buckinghamshire, UK) in a counterbalance design (an experimental design in which all subjects receive treatments to determine the best sequence) with a 7-day washout period between treatments.

To make the test material, 300 mg dried sage leaf and 3 ml of 80% ethanol were placed in a glass container. The mixture was ultrasonically extracted for 10 minutes. The extract was then decanted and filtered. The procedure was repeated twice more. A rotary evaporator was used for 15 minutes to evaporate the solvent, and the flask was weighed to determine the extract's dried weight. The supernatant (clear liquid) was reconstituted with 53% ethanol and assayed for cholinesterase activity.

Subjects underwent a battery of tests and ingested the day's treatment. Then at 1 hour and 4 hours post-dose the participants completed the battery of tests again. The tests included (1) the Defined Intensity Stressor Simulation (DISS) computerized battery, which rates negative mood, arousal, and stress-related physiological responses; (2) the State-Trait Anxiety Inventory (STAI), which measures fluctuating levels of anxiety; and (3) the Bond-Lader visual analogue mood scales, which measures the mood effects of anxiolytics. The dried sage leaf extract was also tested in vitro to assess its AChE activity.

In vitro, sage ethanol extract dose-dependently inhibited AChE and butyrlcholinesterase (BuChE), another similar enzyme. The extract more selectively inhibited BuChE than AChE. BuChE is less specific and is found in plasma and liver, while AchE is found in neuronal tissue and red blood cells (RBC). The authors point out that the activity of sage may also involve other properties yet to be discovered.

In the absence of a stressor, both doses of sage had a significant improvement on ratings of mood ($P < 0.05$). The lower dose reduced anxiety, and the higher dose increased alertness, calmness, and contentedness ($P < 0.05$). Both doses of sage modulated the stress-inducing effects of the DISS battery, but the lower dose was associated with increased anxiety and decreased alertness. The stressful situation eliminated the stress-reducing capability of the low dose of sage. To this end, the authors believe that the lower dose falls below the treatment threshold required to beneficially modulate mood and performance. They believe the higher dose is within the beneficial therapeutic window.

The dose findings in this study are the opposite of that reported in other studies that used the essential oil or ethanolic extracts of *S. lavandulifolia* (Vahl).[3,4] In those studies, the lower dose was within the therapeutic window and the higher dose was not. The authors point out that these divergent findings underscore the lack of current understanding regarding

the consequences of different extraction techniques. The authors conclude that a single 600 mg dose of the dry leaf extract preparation can improve mood and cognitive performance in healthy young individuals. According to Jerry Cott, PhD, a psychopharmacologist at the US Department of Health and Human Services, "There are other explanations for these results that do not involve dose or extraction technique. The primary one is the lack of a specific test for mood and the lack of a concurrent control (placebo) treatment. The results of cognitive tests can change over time when administered on multiple occasions for reasons that may have nothing to do with the treatment" (J. Cott personal communication to C. Cavaliere, June 23, 2006).

As noted just above, preparations from *S. lavandulifolia* have previously shown potential neurological and cognitive benefits in humans. A recent review in *HerbalGram* examined the essential oil and extracts of *S. lavandulifolia* for their potential as a treatment for Alzheimer's disease, based upon the results of multiple studies using these sage preparations.[5]

Sage *Salvia officinalis*
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Such trials monitored the effects of sage on factors thought at that time to be associated either with Alzheimer's symptoms or its prevention, including inhibition of AChE, antioxidant activity, eicosanoid synthesis (part of the inflammatory response), and binding to the estrogen receptor. HG

—Heather S. Oliff, PhD

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Trial Demonstrates that Herbal Combination ColiMil® is Effective for Colicky Infants

Reviewed: Savino F, Cresi F, Castagno E, Silvestro L, Oggero R. A randomized double-blind placebo-controlled trial of a standardized extract of *Matricariae* (sic) *recutita*, *Foeniculum vulgare* and *Melissa officinalis* (ColiMil) in the treatment of breastfed colicky infants. *Phytother Res.* 2005;19:335-340.

Infantile colic, one of the most common problems afflicting 15-30% of Western infants within their first 3 months of life, is of unknown etiology. It is a syndrome characterized by paroxysmal (sudden or spasmodic), excessive, and inconsolable crying. Crying usually starts at the same time each day, being more intense in the afternoon and evening and lasting 2-3 hours. The causes of colic are believed to be organicistic (e.g., "abnormal gastrointestinal function and allergic disorders") and behavioral (e.g., "inadequate and inappropriate maternal–infant interaction").

ColiMil® (Colimil, Milte-Milan, Italy) consists of extracts of lemon balm (*Melissa officinalis* L., Lamiaceae) herb, sweet fennel (*Foeniculum vulgare* Mill. var. *dulce*, Apiaceae) seed, and German chamomile (*Matricaria recutita* L., Asteraceae) flower—herbs known to be effective treatments for gastrointestinal distress and anxiety. The aim of this randomized, double-blind, prospective clinical trial was to evaluate the effect of ColiMil on colicky breastfed infants. The study took place at the Department of Pediatrics of the Regina Margherita Children's Hospital, University of Turin, Italy between March 2001 and March 2003. Infants (aged 21-60 days) diagnosed with severe colic according to Wessel's criteria were divided into 2 groups. According to Wessel's diagnostic criteria, crying lasts for more than 3 hours a day, more than 3 days a week, and for more than 3 weeks. The treatment group received ColiMil (n = 41), and the control group (n = 47) received a placebo (inverted osmosis water, fructose, pineapple flavor, citric acid, and sorbate potassium). Two subjects were withdrawn from the treatment group and 3 subjects from the control group; however, no subject was withdrawn due to "any problems related to the trial." Parents recorded crying time, medication administration, and any observed side effects in a structured diary throughout treatment and after therapy ended for a total of 21 days. Parents also completed a questionnaire at day 21.

Subjects received either the placebo or ColiMil twice a day before breastfeeding for 7 days (2ml/kg/day). Each dose of ColiMil consisted of the following standardized extracts: Sweet fennel fruit powdered extract (PE) standardized to 0.05% to 0.1% essential oil (EO) (164.29 mg), chamomile flower PE standardized to 0.3% apigenin (177.69 mg), lemon balm EO standardized to 2% rosmarinic acid (96.89 mg), 0.85 mg of vitamin B1, 3.24 mg of calcium pantothenate, and 1.20 mg of vitamin B6.

Responders were considered infants whose crying time was reduced by at least 50% per day. Eighty-eight infants completed the trial. At baseline (day 0) daily average crying time was similar between the 2 groups: 201.2 min/day for the ColiMil group (SD 18.3) and 198.7 min/day (SD 16.9) for the placebo group (P=0.507). For the first 3 days of treatment, reduction in crying time was similar between the placebo and ColiMil groups. At day 7, a reduction of crying time was observed in 85.4% of patients receiving ColiMil and in 48.9% of infants receiving the placebo (P<0.005). Average daily crying time at day 7 was 76.9 min/day for the ColiMil group and 169.9 min/day for the placebo group (CI 95% = -102.89, -83.11, P<0.001). Crying was still reduced 15 days after treatment was completed in the ColiMil group (day 21 average daily crying time = 82.1 min/day). Neither group reported adverse side effects.

Based on these results, the authors conclude that ColiMil is a safe and effective treatment for severe colic in breastfed infants. They also suggest that "each component [i.e., each herbal extract] of the phytotherapeutic agent [the formulation] should be evaluated in order to improve the effectiveness of the treatment" and that further studies at different therapeutic doses are needed to determine if this activity is dose-dependent. HG

—Marissa Oppel, MS

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Swiss Horse Chestnut Seed Extract Treats Patients with Chronic Venous Insufficiency: A Review of 5 Clinical Trials

Reviewed: Suter A, Bommer S, Rechner J. Treatment of patients with venous insufficiency with fresh plant horse chestnut seed extract: a review of 5 clinical trials. *Adv Ther.* 2006;23(1):179-190.

Chronic venous insufficiency (CVI) afflicts approximately 6–10% of adults in industrialized countries, and its prevalence increases with age. This disease is characterized by venous stasis resulting from valvular incompetence. Early manifestations of CVI include edema (swelling) of the ankle and calf. Various types of horse chestnut (*Aesculus hippocastanum* L., Hippocastanaceae) seed extract (HCSE) have been used to treat CVI in European countries for decades. Published data support its use for alleviating the pain, cramps, itching, and edema associated with this disease, and the evidence for the efficacy of HCSE has been ample enough to be acknowledged in a positive monograph by the German Commission E.[1]

A recent systematic review of 17 clinical trials on oral preparations of HCSE involving over 1400 patients, has concluded that HCSE is an effective treatment for CVI compared to placebo and reference treatments.[2] The risk/benefit ratio of HCSE for the short-term treatment of CVI was considered positive, with adverse effects being mild and infrequent.

The primary active ingredients of HCSE are collectively known as aescin, which comprise a mixture of alkylated triterpene glycosides. The mechanism of action appears to be an inhibitory effect on the catalytic breakdown of proteoglycans in the cell wall. This article is a review of 5 clinical trials of varying methodological quality on the safety and efficacy of 4 different formulations of HCSE made by the same company (Aesculaforce®; Bioforce AG, Roggwil, Switzerland; marketed in the United States as Venaforce®) in patients with CVI and varicose veins. The 4 Aesculaforce preparations investigated in the 5 clinical trials are described as follows: (1) an alcohol tincture containing 39 mg aescin (the drug-extract ratio of the tincture is 1:2.6; the dosage regimen is equal to 1.5 g of fresh plant); (2) tablets containing 20-mg aescin; (3) tablets containing 50-mg aescin; and (4) gel with 2% aescin (external use). All studies were conducted in compliance with Good Clinical Practice. Changes in several symptoms associated with CVI were assessed, including heaviness and tension in the legs, edema, blue discoloration, pain, burning, and itching. In study 1 (prospective, open, multicenter), 77% of 38 patients had a clinically therapeutic effect after an average of 4 weeks of treatment with the alcohol tincture (25 drops per day), and 60% of the patients rated the efficacy as "good" to "very good" for alleviating leg swelling, pruritus (itching), heaviness and tension in the legs, and cramps.[3] The tincture was well tolerated; 3 adverse

events were reported (2 in the placebo group).

In study 2 (randomized, placebo-controlled, double-blind), symptoms improved in the treatment (20 mg aescin per tablet; 2 tablets per day) and placebo groups (n = 52); ankle circumference decreased significantly more ($P < 0.05$) in the treatment group than in the placebo group.[4] Three reports of gastrointestinal problems were reported (2 in the placebo group and 1 in the treatment group). In study 3 (open, single-center), mean symptom scores improved in all 78 patients after treatment with 50 mg aescin for 8 weeks, 1 tablet per day.[5] Most of the patients (95%) rated the tolerability of the treatment as "good" or "fairly good," and 51% of the patients rated the overall efficacy as "good" or "very good." Several adverse events were reported; however, only 4 were judged to be related to the study medication. In study 4 (open, uncontrolled, multicenter), more than 85% of the patients (n = 64) and physicians rated the overall efficacy of the aescin gel as "good" or "moderate," and 92% of the patients rated the tolerability to be "good."[6] Ankle circumference and mean individual and total symptom scores all decreased significantly ($P < 0.05$). None of the adverse events reported were judged to be related to the study medication. In study 5 (open, uncontrolled), 39 patients completed 8 weeks of therapy with a combination of the aescin gel (applied morning and evening) and the 20-mg tablets (1 per day).[6] All symptom scores decreased by the end of treatment, significantly so for heaviness and pain in the legs and blue discoloration. Efficacy and tolerability scores of between 5 and 8 on a 10-point scale were reported.

The review of these clinical trials concludes that the Aesculaforce® HCSE products, whether taken orally or applied topically, "provide effective treatment for patients with stage I and II CVI, as assessed by both objective and subjective methods" and their effectiveness is comparable with that of standard compression therapy. The products tested were well tolerated and safe, and the authors conclude that "Aesculaforce represents a real alternative therapy for those with mild to moderate forms of venous insufficiency."

A weakness of this review is that it covers both controlled and uncontrolled trial designs, as well as different dosages and modes of administration, e.g., the use of a topical gel vs. tablets for internal use, vs. a combination of both. In addition, 2 of the 3 authors are employed by the manufacturer of the preparations, contributing to potential bias. Nevertheless, the individual trials are each sufficiently powered for their conclusions to be relevant and the results of this review are consistent with those of other trials and reviews of HCSE.[7,8] HG

—Brenda Milot and Mark Blumenthal

Horse chestnut *Aesculus hippocastanum*. Photo ©2006 stevenfoster.com

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Echinacea Taxonomy—Is the Re-classification of the Genus Warranted?

by Mark Blumenthal and Lowell E. Urbatsch, PhD

Systematic botany is primarily concerned with classifying and naming plants, assessing their relationships to one another, as well as gaining insights into the nature of species. In earlier times the lack of a systematic process for determining the names and groupings of plants into families, genera, species, etc., was the source of considerable confusion among botanists, biologists, physicians, pharmacists, herbalists, and others.

In the mid-1700s the Swedish biologist Carl von Linné (Linnaeus) developed what became the modern classification system for plants and animals and the generally accepted method for naming them, i.e., the binomial system of nomenclature.[1] Now generally referred to as the Linnaean hierarchical system of classification, organisms are placed into a series of more inclusive categories such as species, genera, tribes, families, orders, etc., based on their characteristics. In the case of plants, features of their flowers, leaves, fruits, seeds, and now, chromosomes, and so on are evaluated in this regard. Each kind of organism (i.e., all similar individuals that in nature interbreed) is assigned a binomial (genus name plus specific epithet), generally referred to as the species name or scientific name. Similar species are placed in the same genus, similar genera might be grouped in a tribe, and similar tribes within a family.

Since Linnaeus' time and especially within the past 20 years, classification systems have become more rigorous, and also a great deal has been learned about the characteristics of species. Present-day systematic botanists attempt to develop taxonomic categories, (species, genera, families) that are monophyletic (i.e., comprised of organisms descended from a common ancestor). By using nucleic acid technology (DNA), genetics, and plant chemistry, along with traditional taxonomic methods, scientists attempt to show that organisms within a species, genus, family, etc., are related by descent. The many factors used to assess such relationships are highly complex and such data are also subject to the interpretation of scientists who engage in these studies. Species formation itself, meanwhile, is a complex process, generally occurring gradually over thousands to hundreds of thousands of years, frequently causing further complications in assessing species limits (i.e., what individuals belong to a species).

Organisms can be similar to one another for two basic reasons: (1) they are genetically related, or (2) they have independently acquired similar characteristics. For example, certain members of the poinsettia family (Euphorbiaceae) are succulents and look similar to cacti. However, such plants are not closely related genetically, but have independently acquired similar appearances due to their living and coping with the arid environments in which they live. Consequently, placing such succulent species in the same genus, family, or order would produce an improper classification. Similarly, placing George Washington, for example, in someone's family tree because he physically resembles members of that family—but was not shown by birth records to be related—would result in an improper genealogy.

Not only can environment cause similar characteristics and appearances among genetically unrelated plants, it can foster species differentiation among plants that *are* genetically related. Groups of individuals (populations) growing in separate geographic areas often gradually adapt to their particular sites. Over time, they might begin to look different physically and at some point their genetic makeup might change to the degree where individuals from the two sites can no longer interbreed with one another. At this point they would certainly be regarded as distinct species.

Another complexity in assessing species limits involves classifying populations separated geographically that exhibit physical differences but which might interbreed in certain areas where they do grow together. The ability of different plant species to hybridize with one another to a limited extent in nature or extensively under controlled conditions provides important information. It is not uncommon, for example, that many herbaceous species of plants hybridize under controlled conditions and to a limited extent in nature. But the fact that different species can hybridize is not necessarily a basis for concluding that they, in fact, represent a single rather than two or more species.

The stages in species formation are generally thought to be continuous so that the exact point where two differing populations can be regarded as different species is often subject to interpretation. How different in appearance should populations be in order to be called species is a question open to considerable judgment.

Due to the complex nature of species and to the processes of species formation, the systematic botanist is provided a great deal of latitude in interpreting these factors. In non-technical terms botanists are afforded the opportunity to be "lumpers" or "splitters." What might be regarded as weakly differentiated species by some may be thought of as strongly supported varieties by another. However, once a systematic botanist concludes, based on available information, that a species should be reduced in rank to the level of variety or that two species should be combined into one, the rules and recommendations of the International Code of Botanical Nomenclature must be followed in assigning the correct name to the taxon in question. As a result, familiar names that have long been in use could be changed as the result of gaining a better understanding of the plants investigated.

These changes are not simply academic, as they can affect the labeling of commercial products at a considerable cost to publishers and industry, and potentially generate confusion among consumers. The most recent example of the renaming of a commercially popular medicinal plant is the recent renaming of the binomial for black cohosh, the popular Native American plant used to treat symptoms of menopause. Although the popular name (or "standardized common name"[2]) is still "black cohosh," the generally accepted scientific name (binomial) has been changed to that initially given to it by Linnaeus, *Actaea racemosa* L., from *Cimicifuga racemosa* (L.) Nutt., the name that was assigned to this taxon by botanist Thomas Nuttall in 1818.[3] (To possibly complicate matters, particularly for anyone conducting a literature search on the previous medical uses of black cohosh, this herb was referred to as *Macrotys racemosa* by the Eclectic physicians of

the 19th century, a name which itself represents a misspelling of the genus name *Macrotrys*, bestowed on the plant group by C.S. Rafinesque in 1808.)

Echinacea is a medicinal plant of obvious economic importance in the United States, Canada, Europe, and other parts of the world. Although international statistics are difficult to obtain, econometric data from the United States demonstrate the herb's popularity. *Echinacea* (referring to all commercially sold species) was ranked second in total herbal supplement sales in the United States in the Food, Drug, and Mass Market retail outlets, generating over $21 million in revenues in this channel of trade in 2005, according to Information Resources Inc.[4] *Echinacea* is consistently rated the top-selling herbal dietary supplement in health and natural food stores according to SPINS, a market research firm.[5]

The authors of the article on the following pages propose a re-classification of the genus *Echinacea*.[6] This genus is currently regarded as consisting of 9 species as initially proposed by Professor R.L. McGregor in 1968.[7] As noted in the following article, Baum et al propose that these 9 species be "lumped" to 4 species, with the other taxa being termed as varieties of the principal 4 species, based on their prior research and publications on this subject.[8]

For historical perspective, plants in this genus were originally published under *Rudbeckia* by Linnaeus in 1753, later transferred to the genus *Brauneria* in 1790, and then alternatively classed as *Echinacea* in 1794. Both *Brauneria* and *Echinacea* were used until 1959, when *Echinacea* became officially accepted and *Brauneria* was dropped by the 9th International Congress on Botanical Nomenclature.

One of the co-authors of this article (Urbatsch) wrote the section on *Echinacea* for the *Flora North America* volumes on the family Asteraceae (aka Compositae).[9] This treatment is essentially that of McGregor (1968). Based on available information, the McGregor classification was preferable for several reasons. First, floras tend to be more conservative than papers published in scientific journals reporting the results from individual investigations. Second, although Baum et al chose to recognize 4 species of *Echinacea* with others reduced to varietal rank, results from various other investigations (including those of Urbatsch), do not support this conclusion nor, to be frank, do they robustly support any other classification. Relevant published studies based on different data sets differ from one another in the taxonomic conclusions that could be drawn. The extensive AFLP (Amplified restriction Fragment Length Polymorphism) analysis by Mechanda et al (2004)[10] supports neither the McGregor nor the Baum et al reclassification of the genus *Echinacea*. It also serves to vividly illustrate how complex such issues can be. For example, results from the latter study in conjunction with other data could be used to support a classification where 8 species of *Echinacea* might be recognized. Based on Dr. Urbatsch's experience with *Echinacea*, the 8 species classification might be a better alternative than the 4 species proposal by Baum et al. However, it is the opinion of the coauthors of this editorial that at this time the McGregor classification works reasonably well. Presently there is no alternative classification available with substantial support in the botanical taxonomy community. Until such a study is produced, name changes in the genus *Echinacea* should not be made because subsequent changes would most likely be needed. How might such a future classification look? It will probably differ to some extent from that of McGregor; it could be the 4 species scheme proposed by Baum

Continues on page 80

Response from the Authors of Integrating Recent Knowledge about the Genus *Echinacea*

Blumenthal and Urbatsch make arguments for retaining McGregor's (1968) widely used *Echinacea* classification for reasonable arguments of commercial disruption and taxonomic conservatism. We fully agree that it is unnecessary to re-label *Echinacea* products just to be scientifically up to date. On the other hand, we offer the following suggestions to individuals who might want to use the new taxonomy in the future.

McGregor identified the basic groupings of *Echinacea*, which he called species. He based his work on classical examination of herbarium specimens, field populations, and chromosome counts. His choice of species for the grouping was a subjective decision based on his long experience and observations. Our work builds on this important initial observational research by using more objective computerized numerical methods of analysis to sort out statistically different groupings. It is also based on a very large group of individual morphometric characters and features which McGregor did not use (and included phytochemical and molecular characters in separate analyses), taken from many populations of plants throughout the area of their native distribution. The results examine the relationships between populations in a sophisticated way without human bias. The results are very clear. *Echinacea purpurea* is so significantly different from all other species that it is a subgenus. Moreover, among the different analyses conducted on the DNA data, the canonical discriminant analysis strongly supports the 4 species of Binns *et al* 2002 (see Figure 7 in Mechanda et al[1]). The species that McGregor recognized, but which we placed as varieties within our *E. pallida* and *E. atrorubens* complexes, have overlapping populations that are not distinct enough to be rated as fully distinct species according to numerical analysis. So while we agree that *Echinacea* can be classified based on the original McGregor system, it is like viewing the taxonomy of *Echinacea* as a black and white image. Modern methods give us a more sophisticated view. Taxonomy is an unending synthesis that constantly refines previous classifications on the basis of more facts. Why not move up to color? HG

—Bernard R. Baum, PhD; Shannon E. Binns, PhD; and John T. Arnason, PhD

Reference

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Integrating Recent Knowledge about the Genus *Echinacea*:

Morphology, Molecular Systematics, Phytochemistry

by Bernard R. Baum, PhD; Shannon E. Binns, PhD; and John T. Arnason, PhD

Echinacea purpurea
Photo ©2006 stevenfoster.com

Abstract

This article summarizes the authors' recent research on *Echinacea* published in various refereed journals with an emphasis on a new taxonomy. The taxonomy that most people are familiar with is that of McGregor, established in 1968. In these new studies, the authors recognize 4 species in *Echinacea* and have fitted most of McGregor's species as varieties under *E. pallida* and *E. atrorubens,* whereas *E. purpurea* and *E. laevigata* remain as before without varieties. The authors' studies on genomics and phytochemistry have lent support to this taxonomic scheme. This article contains an identification key to the 4 species and to the varieties within *E. atrorubens* and *E. pallida*.

Background

Up until the 1960s, the taxonomy of the genus *Echinacea* was based on specimens that were collected from parts, but not all, of its natural geographical range. Further, before the chemistry of the 1980s and the molecular biology of the 1990s, *Echinacea*'s taxonomic groupings were based on morphology first and subsequently on cytological analyses. For instance, Cronquist described 4 species (and one variety) from his morphological observations of herbarium specimens (including the actual *type* specimens associated with scientific names).[1]

In 1968, R.L. McGregor embarked on a 15-year odyssey studying wild *Echinacea* plants from populations throughout the entire geographical range. His biosystematic studies included the investigation of macro- and micro-morphological traits under a common garden design, and he included some cytological comparisons and some anatomical traits, while making inferences about phylogenetic history, relating to evolutionary development in the genus. McGregor recognized 9 species and 4 varieties.[2] He proposed that there may be extensive genetic variation within certain wild populations of a single species or variety and that further genetic studies were indicated.

Evidence of Phenotypic Variation

Many have relied on McGregor's identification keys to the wild species and varieties.[2] For example, during the herbal medicine boom of the early 90s, botanists, conservationists, and diggers (wildcrafters) used them. Many reportedly found that there was such a large amount of variation between plants of a single population in the genus *Echinacea*, and even between plants of the same age cultivated in a greenhouse, that they were unable to identify the plants confidently. Furthermore, the market demand at that time increased the value of wild roots from *Echinacea angustifolia* (and later from *E. pallida* roots) as well as the aerial parts of *E. purpurea*. There was a dire need for rigorous and accurate morphological identification so dealers could provide certified authentic *Echinacea* to their customers. One solution to the taxonomic problem was the work of Bauer and Wagner; they provided chemical profiles of some secondary metabolites, which were used to distinguish between *Echinacea* and non-*Echinacea* (*Parthenium integrifolium*) dried samples, and they offered some possible means to distinguish between the different species and varieties as well.[3] Bauer and Wagner determined that *E. pallida* (Nutt.) Nutt. var. *pallida*, Asteraceae [syn. = *E. pallida* (Nutt.) Nutt.] was being cultivated and sold erroneously as *E. pallida* (Nutt.) Nutt. var. *angustifolia* (DC.) Cronq. [syn. = *E. angustifolia* DC. var. *angustifolia*]. Building on Bauer and Wagner's discovery of potential chemotaxonomic traits in the commercial species, we undertook a large-scale taxonomic molecular and phytochemical revision. Our goal was to ensure more accurate botanical identification of all the different *Echinacea* taxa for reasons of safety in the supply chain for phytomedicines and for reasons of wild rare species conservation.

Conservation of the natural *Echinacea* resources across North America has socio-political implications due to issues of private and public land tenure, especially on Aboriginal (i.e., Native American) land reserves. Governance of lands and natural resources tends to vary at the federal, state/provincial, or regional levels in both Canada and the United States. The majority (>90%) of natural *Echinacea* populations occur in the United States (see Figure 1 below), where there is a National Germplasm Conservation Program that addresses all *Echinacea* taxa among other resources and threatened species in collaboration with the Nature Conservancy, the State Departments of Natural Heritage/Conservation, and the US Department of Agriculture (USDA).

Morphological Systematics

In an attempt to rectify the situation of poor botanical identification methods with *Echinacea* on the market, we studied 110 wild populations (see Figure 1 below) to gauge the extent of variation between plants in a population and between populations in a species. Our objective was to investigate taxonomic groupings based on the degree of morphological similarity between plants, and to test the statistical significance of our resulting groupings using morphometric tools.

Methods

Natural populations were taxonomically identified in the field according to McGregor,[2] and transplanted to a greenhouse for morphometric data collection.[4,5,6] We measured 74 traits for over 300 specimens, which allowed us to calculate the statistical index of similarity between (1) individual plants (assuming no prior taxonomic groups), and (2) McGregor's taxonomic groups. We used a Gower coefficient of similarity (a biostatistical measuring tool),[7] followed by several clustering methods, and canonical discriminant analyses to assess the groupings.[4]

Findings

The morphometric analyses supported 2 acceptable cluster solutions. The first strongly supported 2 major taxa within *Echinacea*, which we determined to be at subgenus level. The species known currently as *E. purpurea* (L.) Moench was the sole taxon in

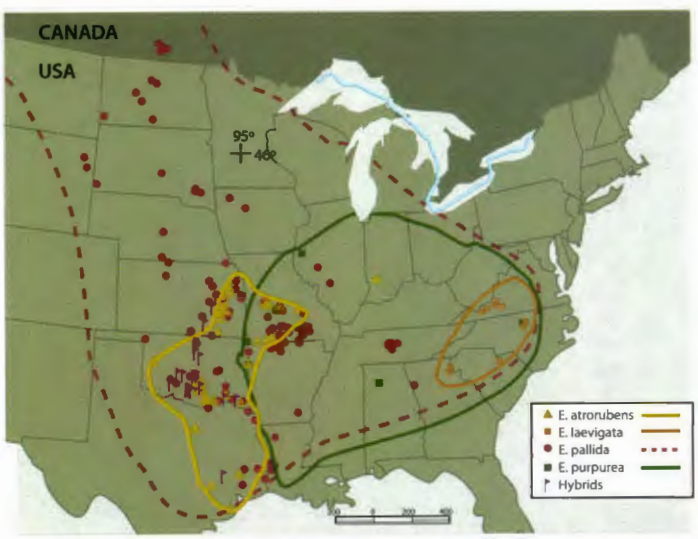


Figure 1. Map of *Echinacea* species sampled throughout most of the range of the native populations of this genus in 1998-1999 for several integrated studies presented herein (reprinted from Binns *et al*[4]).

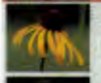
Echinacea subgenus *Echinacea* which contains only *E. purpurea*, whereas all other infrageneric taxa were in *Echinacea* subgenus *Pallida*. The second most acceptable cluster solution supported 4 taxa, which we determined to be at the species level: (1) *E. purpurea* [= *Echinacea purpurea* (L.) Moench *nom. cons. prop.*],[8] (2) *E. laevigata* [= *E. laevigata* (Boynton & Beadle) Blake], (3) *E. atrorubens*, and (4) *E. pallida*. Therefore, we effectively re-classified the genus *Echinacea* into 2 subgenera, one with a single species in it, and the other having 3 species. Our results also supported an 8 cluster solution using McGregor's identification keys.[2] The 8 groups correspond to varieties within 2 species (see Table 1). The revised taxonomy recognizes all of McGregor's taxa, except for one variety, *E. angustifolia* DC. var. *strigosa* McGregor, which was not distinct from *E. pallida* var. *angustifolia*. This putative variety may be a morphotype that resulted from introgression [movement of alleles from one taxon to another through hybrid intermediates, usually found in populations bordering and/or overlapping each other], and it shows the same phenotype [the visible, measurable characteristics, which may vary independent of genetic makeup] in similar ecological zones.[8]

Identification Key for *Echinacea* Species and Varieties

A dichotomous identification key is used by biologists to identify organisms to different levels, such as family, genus, species, or variety. It is designed to list traits of organisms as a series of paired choices that lead progressively to identification of the organism. Not all keys lead to the same level of taxonomic identification, and it is important to have all traits match the key statement that is chosen for any given specimen in order to arrive at the most accurate identification of that organism. In the key below, one may proceed to take a plant or specimen in question and choose between the pair of statements numbered with "1," which then leads *either* to a choice between a pair of "2" statements (and eventually identification of plants in the subgenus *Pallida*), or to identify the plant in question as subg. *Echinacea*, *E. purpurea* (L.) Moench. If one continues to follow the number at the end of the statement that is true, one will eventually arrive at the best identification of that particular specimen. Note that if some traits in the key are not observable in the specimen in question, then another specimen with those missing organs must be used for the key to function properly.

1. Basal leaf up to 5 cm wide; cauline leaf 0.5 to 4.5 cm wide; taproot (may be branching or fusiform); leaf blade trichomes multicellular with knobby joints; major veins almost parallel from a common origin at the base; 1-3 series of involucral bracts..... 2. subg. *Pallida*
1. Basal leaf greater than 5 cm wide; cauline leaf 4.5 to 9 cm wide; fibrous roots (from a caudex); leaf blade trichomes bicellular with ledge-like joints; major veins branched; four series of involucral bracts.....subg. *Echinacea*, *E. purpurea* (L.) Moench
    2. Basal leaf greater than 3 cm wide; basal leaf margin serrate, or dentate; adaxial leaf blade stalked trichomes absent; stem stalked trichomes absent; cauline leaf margin serrate ..... *E. laevigata* (C.L. Boynton & Beadle) Blake
    2. Basal leaf up to 3 cm wide; basal leaf margin entire; adaxial leaf blade stalked trichomes present; stem stalked trichomes present; cauline leaf margin entire 3
        3. Stem stalked trichomes appressed (strigose); leaf blade stalked trichomes sparse; leaf marginal trichomes different than blade trichomes (more appressed). 4
            4. Ray floret yellow..... *E. atrorubens* Nutt. var. *paradoxa* (J. B. Norton) Cronq.
            4. Ray floret pale pink to purple, or white 5
                5. Disk corolla petal fusion more than 3/4 total corolla length; involucral bract up to 0.2 cm wide; stem branched....*E. atrorubens* Nutt. var. *atrorubens* Cronq.

Table 1. Taxonomy of McGregor[2] compared to the revised taxonomy of Binns et al[4] for species and varieties of genus *Echinacea*.

McGregor (1968)	Binns et al (2002)
 *E. purpurea* Photo ©2006 stevenfoster.com	 *E. purpurea*
 *E. pallida* Photo ©2006 stevenfoster.com	 *E. pallida* var. *pallida*
 *E. angustifolia* Photo ©2006 stevenfoster.com	 *E. pallida* var. *angustifolia*
 *E. sanguinea* Photo©2006 Tom Barnes, University of Kentucky.	 *E. pallida* var. *sanguinea*
 *E. simulata* Photo ©2006 stevenfoster.com	 *E. pallida* var. *simulata*
 *E. tennesseensis* Photo ©2006 stevenfoster.com	 *E. pallida* var. *tennesseensis*
 *E. atrorubens* Photo ©2006 stevenfoster.com	 *E. atrorubens* var. *atrorubens*
 *E. paradoxa* Photo ©2006 stevenfoster.com	 *E. atrorubens* var. *paradoxa*
 *E. paradoxa* var. *neglecta* Photo ©2006 stevenfoster.com	 *E. atrorubens* var. neglecta
 *E. laevigata* Photo ©2006 stevenfoster.com	 *E. laevigata*

5. Disk corolla petal fusion less than 3/4 total corolla length; involucral bract greater than 0.2 cm wide; stem unbranched ..*E. atrorubens* Nutt. var. *neglecta* (McGregor) Binns B. R. Baum & Arnason

3. Stem stalked trichomes hirsute, or straight pubescent; leaf blade stalked trichomes dense; leaf marginal trichomes identical to leaf trichomes in type and habit 6

6. Ray floret up to 4 cm long 7

7. Capitulum up to 2.5 cm wide; involucral bract up to 0.2 cm wide ..... *E. pallida* (Nutt.) var. *tennesseensis* (Beadle) Binns B. R. Baum & Arnason

7. Capitulum greater than 2.5 cm wide; involucral bract greater than 0.2 cm wide ..... *E. pallida* (Nutt.) var. angustifolia (DC.) Cronq.

6. Ray floret greater than 4.0 cm 8

8. Fresh pollen white ... *E. pallida* (Nutt.) Nutt. var. pallida

8. Fresh pollen yellow, or lemon 9

9. Ray achene trichomes present; stem unbranched. ..... *E. pallida* (Nutt.) var. *simulata* (McGregor) Binns B. R. Baum & Arnason

9. Ray achene trichomes absent; stem branched. ..... *E. pallida* (Nutt.) var. *sanguinea* Gandhi & Thomas

Related information for identification of species and varieties (including an interactive key, and alternative key with McGregor's taxonomy) may be found on the Web site of Agriculture Canada (http://res2.agr.gc.ca/ecorc/echinacea/key-cle_e.htm). This will eventually be modified online to allow for identification from separate plant parts. To identify a whole plant, one can choose one of the alternative descriptions at number 1 and then follow the leads.

Evolutionary hypotheses

The greatest amount of morphological and genetic diversity observed among geographically-close populations was found in a narrow region of the Great Plains, which is considered by field botanists to be the center of *Echinacea* diversity.[4,9] The "center of diversity" spans several eco-regions that share characteristics of having overlapping biogeoclimatic "edges," such as tallgrass prairie abutting limestone upland formations and/or shortgrass prairies. The following areas are included in the hypothetical region: Ozark Mountains of Missouri and Arkansas, prairies of Kansas and Oklahoma, and especially Black Hills of southeastern Oklahoma where suspected hybridization and introgression may be directing the most active speciation within the genus.[4,9]

In our work, the evolutionary relationships between the 4 revised species were estimated using a cladistic analysis [based on shared, derived characters which are often also diagnostic] of 36 characters (including some phytochemical ones). See the cladogram [an evolutionary tree] (see Figure 2 right), where *Echinacea* is distinguished phylogenetically from the outgroup [a sister group] *Rudbeckia* (98% bootstrap value) [a method for assessing the statistical significance of the relationships between taxonomic groups, i.e., positions of branches in an evolutionary tree]. Within the *Echinacea* clade, *E. atrorubens* and *E. pallida* share 3 unique, derived characteristics, and *E. purpurea* was most basally divergent. Although historically *E. laevigata* was confused with *E. purpurea*,[10] current morphometric results show it to be closely related to *E. pallida* and *E. atrorubens*.

In summary, we proposed a hierarchy of 2 subgenera, 4 species and 6 varieties in the genus *Echinacea*.[4] The 2 subgenera are novel, but our results confirm the 4 species groups that were first suggested using classical taxonomic methodology.[1] All of our described varieties were previously either species or varieties according to McGregor.[2] Table 2 on page 37 compares the classifications of both McGregor[2] and Cronquist[1,11,12] to the revised taxonomy.[4]

Molecular Systematics Based on DNA Methods of Purple Coneflowers: Genus *Echinacea*

How does this genus of Purple Coneflowers fit with the other Coneflower genera?

Echinacea is a genus classified in the Heliantheae tribe within the family Asteraceae. Together with other genera in this tribe, *Echinacea* plants are popularly known to be among the "Coneflowers." The relationship of the genus *Echinacea* to others has been studied using techniques which aim to determine the degree of relationship and the probable evolutionary development of these plants over time. For example, an article published in 1995 by Urbatsch and Jansen reported restriction site analysis of the chloroplast genome, which placed the genus in the subtribe Ecliptinae.[13] This subtribe is distinct from, yet closely related to, Rudbeckiinae, which contains the genera *Dracopsis*, *Ratibida*, and *Rudbeckia*.[14,15] Subsequently, Urbatsch *et al* used another approach, nuclear rDNA internal transcribed spacer (ITS) sequences, to study evolutionary relationships among the Coneflowers and relatives and also to combine the data with their previous chloroplast DNA restriction site data.[16] They concluded that *Echinacea* ought to be classified within the tribe Zinniinae, and that it is definitely *not* related to genera in the Rudbeckiinae.

In the cladogram of the combined data they used 6 species (*sensu* McGregor 1968) of *Echinacea* with similar results of relationships among species as in the chloroplast DNA restriction site data, i.e., that *E. purpurea* is closely related to *E. paradoxa*.

Species and varieties of *Echinacea*

Using Amplified restriction Fragment Length Polymorphism (AFLP®, see side bar on page 36), Mechanda *et al*[17] undertook a study in parallel to Binns *et al*[4] to seek independent support for the morphologically based classification (including relationships) and to complement it in 2 respects: (1) to estimate the genetic

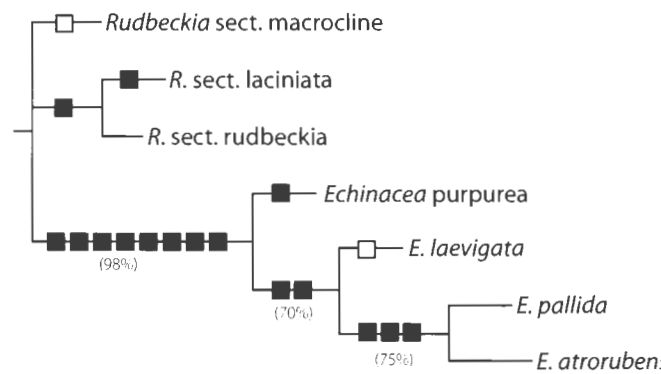


Figure 2. Cladogram of *Echinacea* species (reprinted from Binns *et al*[5]). A 40-step most parsimonious cladogram representing the monophyletic genus *Echinacea* Moench compared to 3 sections of *Rudbeckia* in an outgroup. Confidence intervals are indicated in brackets below the branches (bootstrap values using the 50% majority-rule consensus method). Cladistic analysis was performed with 36 characters (Binns *et al*[4]). Dark boxes signify synapomorphies and empty boxes signify parallelisms.

diversity of the species and varieties, and (2) to provide means of identification of single plants by DNA fingerprinting.

Four hundred thirty-five individual plants were sampled from 58 natural populations representing both the area of distribution and the species and varieties of both Binns *et al*[4] and McGregor[2] classifications. The most notable outcome resulting from the AFLP investigation was that each individual could be uniquely distinguished by a combination of presence/absence of a set of 124 fingerprints. The main finding of this study was support for the 4 species classification of Binns *et al*,[4] but not for all the varieties, most of which were previously recognized by McGregor as species.[2] The species are recognized by a combination of DNA fingerprints, not by a single or a few single and unique AFLP bands. Thus, to identify an individual plant to species with AFLP one needs to resort to more elaborate means, as indicated in Mechanda *et al* with an example (refer to Table 11 in their article).[17] In the example, 10 DNA bands from a single primer set are apparently sufficient to identify an unknown plant, or plant fragment, to one of the 4 recognized species.

As far as relationships among the 4 species are concerned, although no attempt was made to use any outgroup (a reference outside *Echinacea* but close enough to it) in the AFLP study, *E. laevigata* and *E. purpurea* can be construed as forming a sister group based on the unrooted UPGMA dendrogram (refer to Figure 4 in Mechanda *et al* 2004,[17] which is not a true phylogenetic tree). This can easily be seen when moving the branches of the dendrogram without changing the topology. Based on this the genus *Echinacea* consists of 2 parallel pairs: *E. purpurea-E. laevigata* and *E. atrorubens-E. pallida*. This finding supports the gross morphological similarity seen between at least the first two, since they have sometimes been confused.[8,10]

The gene diversity of all the species together in the genus and similarly for the varieties together (measured on a scale from 0 to 1) was nearly 0.5 for both. The species with highest gene diversity was *E. purpurea*, also near 0.5 whereas the 3 other species had lower rates at 0.3. Both *E. purpurea* and *E. laevigata* do not contain varieties. Although the varieties were not supported by the AFLP results, when analyzed for genetic diversity, those of *E. pallida* had greater values than those of *E. atrorubens*, with the exception of *E. pallida* var. *tennesseensis* having the lowest genetic diversity (near 0.2), which is understandable due to its rarity with limited individuals in the populations (*E. pallida* var. *tennesseensis* is currently listed as a federally endangered species by the US Fish and Wildlife Service[18]). The genetic variation was apportioned as follows: 19% among species, 40% among populations within species, and 41% within populations. In other words, the genetic variation among populations was found to be about equal to the genetic variation within populations. But obviously the kind of variation was different since every individual was found to possess unique fingerprints.

Once you know it's *Echinacea*, how do you determine what kind of *Echinacea* it is?

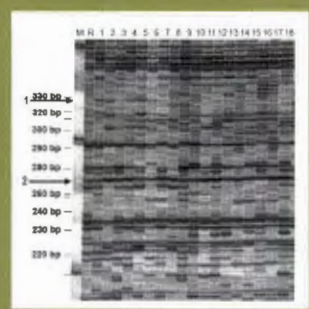
There were major difficulties in identification of plant materials that were reported by wildcrafters, growers, and scientists during the early days of *Echinacea*'s boom in the commercial marketplace (see Morphological Systematics section on page 33). For this reason, 2 collaborating research teams used modern tools in both morphometric taxonomy[4] and molecular systematics[17] to discover which natural taxonomic groups exist currently in wild plant populations. Mechanda *et al* distinguished wild species and varieties in *Echinacea* using Amplified restriction Fragment Length Polymorphism (AFLP®).[17] This generated results about relationships between plants and populations based on DNA. Also, it allowed for independent support for the morphological classification by complementing it in 2 respects: (1) it estimates the genetic diversity of all types of *Echinacea* species and varieties growing in the wild, and (2) it provides a means for stakeholders to identify and trace single plants by DNA fingerprinting.

How are the different kinds of *Echinacea* species and varieties related?

Based on work by Mechanda *et al*, the genus *Echinacea* consists of 2 parallel pairs: *E. purpurea-E. laevigata* and *E. atrorubens-E. pallida*. *E. laevigata* and *E. purpurea* can be construed as forming a sister group based on the unrooted UPGMA dendrogram (see Figure 4 in Mechanda *et al* 2004, which is not a true phylogenetic tree).[17] In this approach, no attempt was made to use any

Amplified restriction Fragment Length Polymorphism (AFLP)

AFLP™ is one of a number of DNA techniques used to reveal fingerprints. The figure below is an example of a number of DNA profiles, i.e. each lane is a fingerprint of an *Echinacea* plant. To obtain such a profile the investigator first cuts the DNA with 1 or 2 enzymes. Then the investigator attaches a small stretch of DNA, called adaptor, to each of the resulting DNA fragments. In the next step the investigator adds a single nucleotide to the 2 adaptors, resulting in 2 primers. These 2 primers are used to amplify the DNA that was cut in the previous step in a PCR reaction. This results in a 16-fold reduction of the total fragments being amplified. In the next step another 1 or 2 nucleotide(s) are added to the primers, resulting in 2 new primers. Amplification with 2 nucleotides added result in a 256-fold reduction of DNA bands. The reason for the reduction of DNA bands is to obtain a relatively small amount of bands that is manageable as in the figure and enough to find differences among fingerprints. Once amplified, the DNA fragments (bands in short) migrate differently according to their weight (nucleotide base pairs) when subjected to an electric field. To visualize the resulting DNA fragments, the investigator needs also to label them in order to detect them. This is done with a fluorescence dye and run in specially designed equipment such as a DNA sequencer, or radioactively labeled and then run on an acrylamide gel. When run on a gel, it is photographed, the result of which is shown in the figure above.



In the figure each lane represents a single Echinacea plant (labeled 1 to 18 in this example). An example of DNA fragments that migrate differently are shown with arrow #1, whereas examples of fragments that migrate the same are shown with arrow #2. M indicates the DNA marker with the corresponding fragment sizes shown. The smaller fragments are the lower ones. R indicates a reference individual used in every gel.

Photo taken from Mechanda *et al*[17] by permission.

outgroup comparison, and the tree is not a true phylogenetic tree (as seen by the unchanging topology when branches in the tree are rotated). This finding supports the gross morphological similarity seen between *E. purpurea* and *E. laevigata*.[8,10]

Both *E. purpurea* and *E. laevigata* do not contain varieties. The other 2 species, *E. pallida* and *E. atrorubens,* each contain varieties by morphometric classification,[4] but classification by AFLP results did not resolve distinct groups at the variety level. In fact, genetic diversity was measured on a scale of 0 to 1 and found to be 0.5 among species, and also 0.5 for all varieties together. The species with highest gene diversity was *E. purpurea*, near 0.5, and the 3 other species had lower rates at 0.3. Varieties of *E. pallida* had greater diversity ratings than those of *E. atrorubens*, with the exception of the rare *E. pallida* var. *tennesseensis* having the lowest genetic diversity (near 0.2).

Although hybrids and hybrid populations were reported by McGregor,[2] we were unable to distinguish them from others by genetic diversity measured with AFLP analysis, although more than one suspected hybrid population in the field was identified in the morphometric work by Binns *et al*.[4]

Other DNA work done on *Echinacea*

Urbatsch and Jansen only studied 7 of the 9 *Echinacea* species recognized by McGregor[2] and found that *E. purpurea* was closely related evolutionarily to *E. atrorubens* and *E. paradoxa,* and that *E. simulata* was possibly the more ancestral species.[13] Later, Urbatsch *et al* reported combined data analysis using 6 species of *Echinacea* (*sensu* McGregor 1968).[16] Their cladogram shows similar relationships among species to those in the Urbatsch and Jansen paper on chloroplast DNA restriction site data,[13] i.e., *E. purpurea* is closely related to *E. paradoxa*.

As part of our AFLP study we found that the AFLP fingerprints were inappropriate for phylogenetic studies.[17] However, Kim *et al* carried out a similar AFLP study to ours, with much less sampling to assess phenetic/phylogenetic relationships among *Echinacea* species and varieties (sensu McGregor).[19] Their results, not surprisingly, did not provide support for the presently accepted classification by Binns *et al*.[4] One reason for this is that AFLP data are usually inappropriate for phylogenetic studies demonstrated on theoretical grounds, as explained by Clark and Lanigan[20] regarding RAPD data. Clark and Lanigan's explanation equally applies to AFLP data in many respects, including ours (refer to the Discussion section on "Phylogenetic analysis," pages 480-481 in Mechanda et al[17]). Another reason is that the identification of their material may be questionable, especially if they relied on McGregor's keys, which have been problematic in the past.[4] A different investigation was carried out by Kapteyn *et al* using DNA-RAPD.[21] RAPD has proven to be less amenable to reproducibility than AFLP. Kapteyn *et al* used only the 3 main commercial species (*E. angustifolia*, *E. pallida*, and *E. purpurea*) and their study remained inconclusive.[21]

How can DNA markers be used to authenticate sample materials of *Echinacea* species and commercial lines (cultivars?) within species?

That authentication of commercial material of *Echinacea* is of prime interest to the consumer goes without saying. Authentication is needed to ensure the correct and proper content of the product. Correct identification of the plant material constitutes one aspect, and correct phytochemical characterization of plant extracts is another aspect (i.e., the quantitative analysis of marker phytochemicals for assurance of safety, quality, and potentially of therapeutic value). Both are needed in the natural health products industry. The study by Mechanda *et al* has shown the poten-

Table 2. Taxonomic treatments of *Echinacea* Moench by McGregor,[2] Cronquist,[1,11,12] and Binns, Baum, and Arnason.[4]
Synonyms are in square brackets []. Permission to reprint Binns © 2001 University of Ottawa.

McGregor	Cronquist	Binns, Baum, and Arnason
1. *E. angustifolia* DC. var. *angustifolia* *E. angustifolia* DC. var. *strigosa* McGregor	1. *E. pallida* (Nutt.) Nutt. var. *angustifolia* (DC.) Cronquist [*E. angustifolia* DC. var. *strigosa* McGregor]	1. *E. pallida* (Nutt.) Nutt. var. *angustifolia* (DC.) Cronquist *E. angustifolia* DC. var. *strigosa* McGregor]
2. *E. tennesseensis* (Beadle) Small	[*E. tennesseensis* (Beadle) Small]	*E. pallida* (Nutt.) Nutt. var. *tennesseensis*
3. *E. pallida* (Nutt.) Nutt.	*E. pallida* (Nutt.) Nutt. var. *pallida*	*E. pallida* (Nutt.) Nutt. var. *pallida*
4. *E. simulata* McGregor	[*E. simulata* McGregor]	*E. pallida* (Nutt.) Nutt. var. *simulata* (McGregor) Binns, B. R. Baum & Arnason
5. *E. sanguinea* Nutt.	[*E. sanguinea* Nutt.] (suggested variety)	*E. pallida* (Nutt.) Nutt. var. *sanguinea* (Nutt.) Gandhi and Thomas
6. *E. atrorubens* Nutt.	2. *E. atrorubens* Nutt. var. atrorubens	2. *E. atrorubens* Nutt. var. *atrorubens*
7. *E. paradoxa* (Norton) Britton var. *paradoxa* *E. paradoxa* (Norton) Britton var. *neglecta* McGregor	*E. atrorubens* var. *paradoxa* (Norton) Cronquist	*E. atrorubens* Nutt. var. *paradoxa* (Norton) Cronquist *E. atrorubens* Nutt. var. *neglecta* (McGregor) Binns, B. R. Baum & Arnason
8. *E. laevigata* (Boynton & Beadle) Blake	3. *E. laevigata* (Boynton & Beadle) Blake *nom. cons. prop.*	3. *E. laevigata* (Boynton & Beadle) Blake nom. cons. prop.
9. *E. purpurea* (L.) Moench	4. *E. purpurea* (L.) Moench *nom. cons. prop.*	4. *E. purpurea* (L.) Moench *nom. cons. prop.*

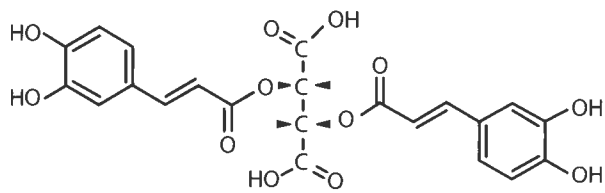
tial of correct identification to species.[17] In another study, the use of DNA-based markers to predict phytochemical profiles in extracts of identical material were assessed by Baum *et al*, using AFLP and High Pressure Liquid Chromatography (HPLC).[22] In this study, we determined both AFLP DNA fingerprints as well as the quantitative profiles of 2 marker compounds, namely, cichoric acid (2,3-*O*-dicaffeoyltartaric acid) and dodeca-2E, 4E, 8Z, 10E/Z-tetraenoic acid isobutyl amide in over 50 accessions of *E. purpurea*. This small study has shown the potential of DNA markers to predict the amount of industry marker chemicals. An extension of this study or a similar DNA-based study may be needed to distinguish the true product from adulterants (wrong plant species, wrong plant line, wrong plant part) and contaminants (like bacterial or fungal, foreign matter).

Phytochemical Variation of *Echinacea* in Wild Populations

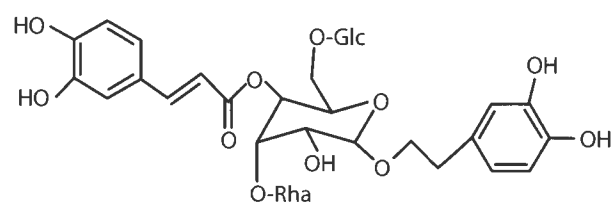
The phytochemistry of *Echinacea* species is of key importance to the herbal industry because the phytochemical markers are some of the most easily identifiable characters for species identification in processed products. Also, they are biologically active substances that have importance in the pharmacology of the products. The basic phytochemistry of *Echinacea* was undertaken in Germany at a time when there was little interest in North America in this medicinal endemic prairie genus.[3,23] The main groups of importance are caffeic acid derivatives (CADs) (see Figure 3 below), lipophilic alkamides (AAs) and ketoalken/ynes (see Figure 4 on page 39), although other types of secondary metabolites are also found in the genus.

It is well known in chemosytematics that individual species are likely to have their own unique blend of phytochemicals, developed in the co-evolutionarily-driven progression towards developing novel defense chemicals. Bauer showed that this principle can be used to distinguish the 3 commercial *Echinacea* taxa by HPLC analysis if other species/varieties are not considered as possible components of a mix.[3,23] Moreover, in *Echinacea*, there is a high degree of phytochemical redundancy in individual species, i.e., they contain 5 or more CADs and 10 or more AAs. As a result of phytochemical research, unique marker phytochemicals have been used qualitatively to certify botanical identification in the industry. Commercial species/marker relationships used in industry are as follows: echinacoside as a marker for *E. pallida* var *angustifolia* versus *E. purpurea*, and the use of ketoalkene/ynes as markers for *E. pallida* var *pallida*.

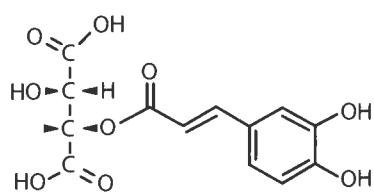
The recent revision of the genus *Echinacea* and the detailed study of phytochemistry of all the species and varieties from wild and cultivated sources reveal a more complex picture.[4] This is important to the herbal industry for the purpose of assessing contamination of commercial seed lots with wild species or the use of wildcrafted species of doubtful origin in the product. The phytochemical variation also supports the morphometric classification of different taxa within the genus by Binns *et al*,[5] but the identification of all the species and varieties using phytochemistry is confounded by polyploidy [having more than 2 sets of chromosomes which are homologous (same genes, not necessarily the same gene products/functions)] and cannot be achieved solely on the basis of presence or absence of one or a few compounds. The major findings follow.



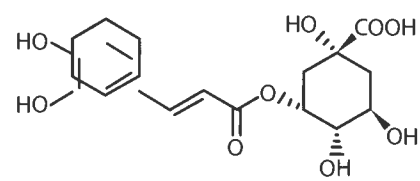
Cichoric acid
(2,3-*O*-dicaffeoyl tartaric acid)



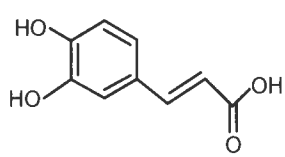
Echinacoside



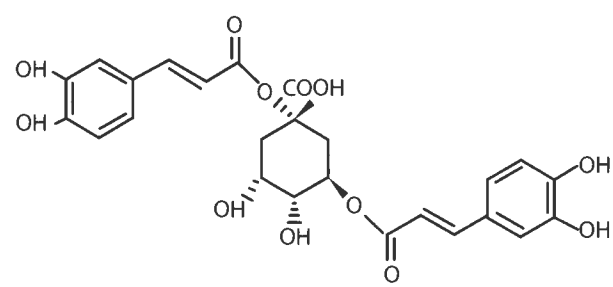
Caftaric acid
(2-*O*-caffeoyl tartaric acid)



Chlorogenic acid
(3-*O*-caffeoyl quinic acid)



Caffeic acid



Cynarin
(1,3-dicaffeoyl quinic acid)

Figure 3. Caffeic acid derivatives in *Echinacea* species and varieties.

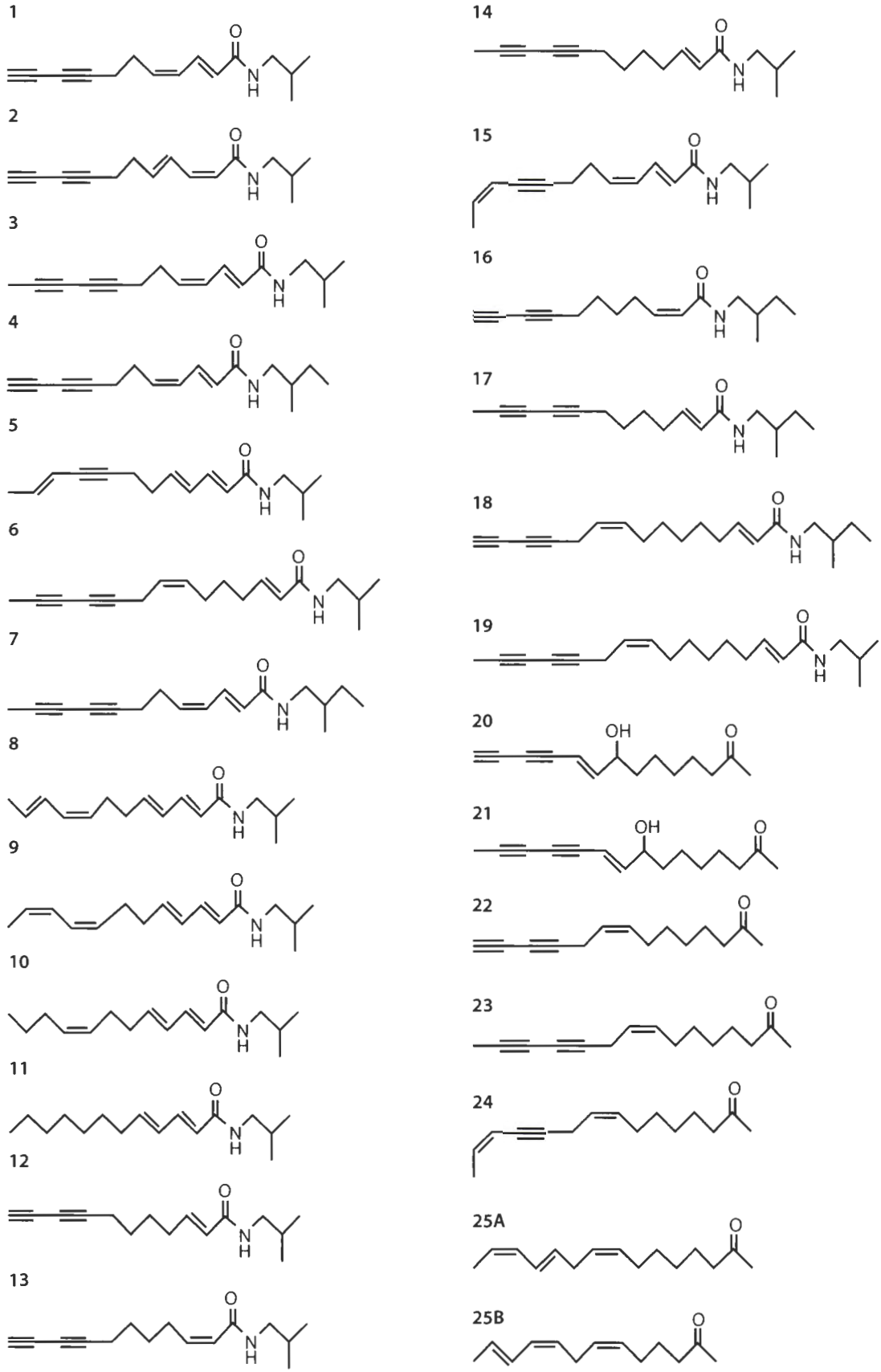
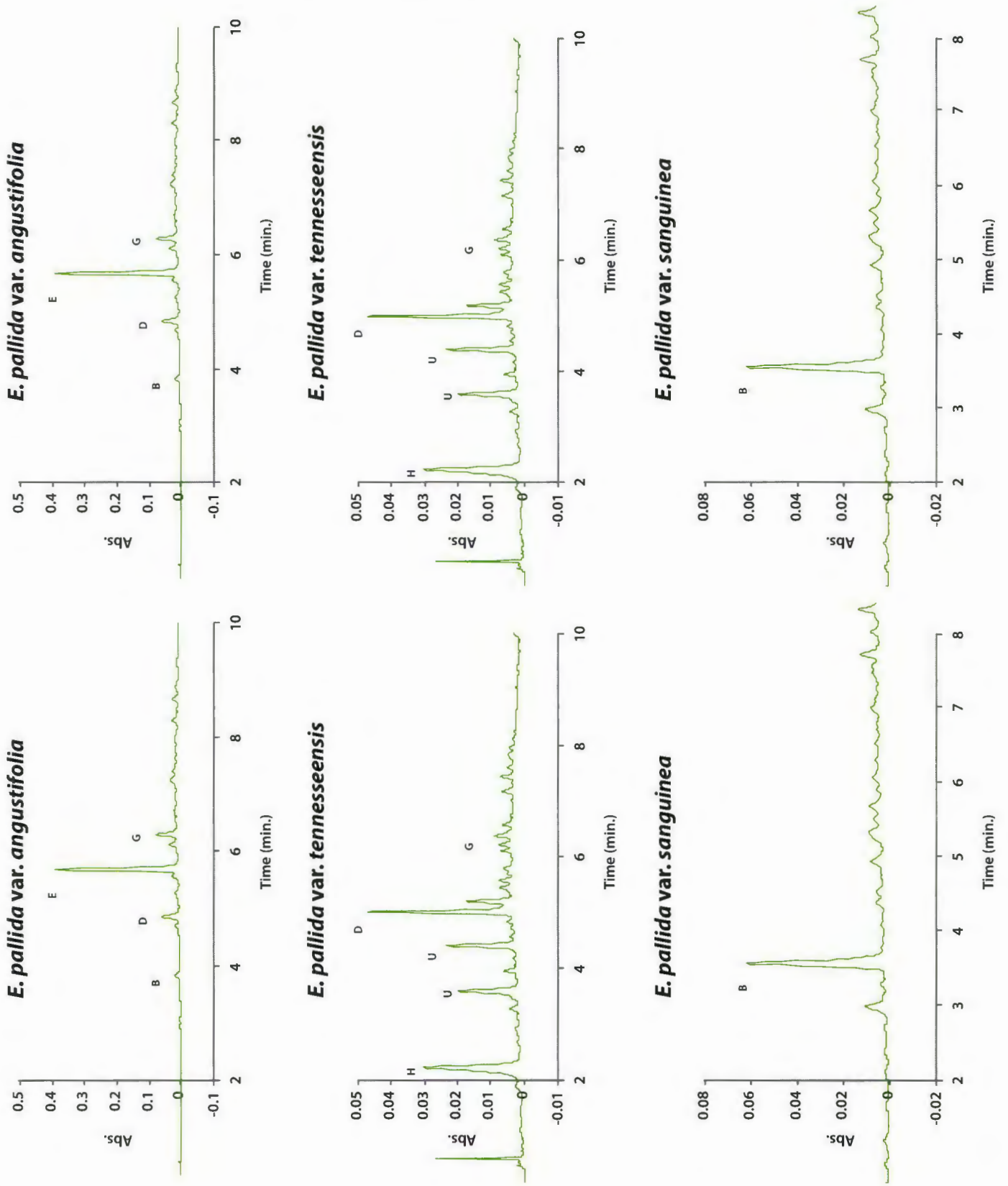


Figure 4. Alkamides and ketoalken/ynes in *Echinacea* species and varieties.

The current industry practice, which uses echinacoside as a positive marker for *E. pallida* var. *angustifolia* versus *E. purpurea* where it is absent, is an over simplification if all species and varieties are considered. In fact, echinacoside is present in quantifiable amounts from roots of all *Echinacea* taxa except *E. purpurea*; namely, 3 species and 7 varieties.[4,5] Trace amounts of echinacoside were found in *E. purpurea*, so lack of this compound is not the best marker. The absence of alkamide 18 was found to be a more definitive *E. purpurea* marker.

Ketoalkenes/ynes cannot be taken as definitive markers for *E. pallida* var. *pallida*, as often considered in industry practice. However, they do appear to be markers for polyploids. They are found not only in *E. pallida* var. *pallida* but also in *E. pallida* var. *simulata* which is sometimes triploid, as well as possibly hybridizing populations of *E. atrorubens* var. *neglecta* and *E. atrorubens* var. *paradoxa*.



On a positive note, the species and varieties are readily distinguishable on the basis of quantitative HPLC (high-performance liquid chromatography) profiles of the compounds (see Figure 5 on pages 40 and 41 and Figure 6 on page 42 and 43), but not generally on the presence or absence of individual compounds; notably, the roots of *E. angustifolia* and *E. pallida* can be differentiated by the occurrence of the CADs, 1,3-0-(cynarin) and 1,5-0-dicaffeoylquinic acids present only in the former.[24] Canonical discriminant analysis revealed that cichoric acid, the diene AAs 1-3 and 7, and ketoalkene 24 were the best taxonomic markers. HPLC profiles for the lipophilic compounds contain more information because they contain a larger number of compounds.

Plant age (and plant part) generally changes the expression of compounds. Young plants expressed lower amounts of alkamides in roots and flowers than present in older plants. Levels of compounds in young roots can also be increased significantly by induction with methyl jasmonate, which suggests they are also inducible by mechanical, insect, or fungal damage.[25]

In other studies we showed that the quantitative presence of phytochemicals, such as 8,9 and cichoric acid in mature plants, can be correlated to DNA markers (AFLPs) across a wide variety of *Echinacea* germplasm.[22] This indicates that DNA markers may be useful in screening germplasm for active principles where phytochemistry may be less easy to assess.

In another study, Binns *et al* addressed the question of how much phytochemical variation is naturally present within and between wild populations.[10] This is important for the wild harvest of seed for sale or cultivation, and the continued wild harvest of *Echinacea* populations from certain areas within the native range of these plants. *E. pallida* var. *angustifolia* was chosen for study because it has the largest latitudinal spread of any species/variety and occurs from Manitoba to Texas. There was significant variation in AAs and CADs between populations studied, which may support the existence of distinct chemoraces in this variety.[10] Fortunately this variation is largely quantitative, and does not alter the phytochemical profile needed to identify the species. Also, since these experiments were conducted on seeds from the range of this variety, grown in uniform conditions, the variation measured was more likely to be genotypic rather than phenotypic, or caused by environmental influences.

Along with (North) American ginseng (*Panax quinquefolius* L., Araliaceae) *Echinacea* is possibly North America's most important ethnobotanical product. Since it originates from here, the North American industry must contend with the genetic diversity associated with the center of origin of this medicinal crop.

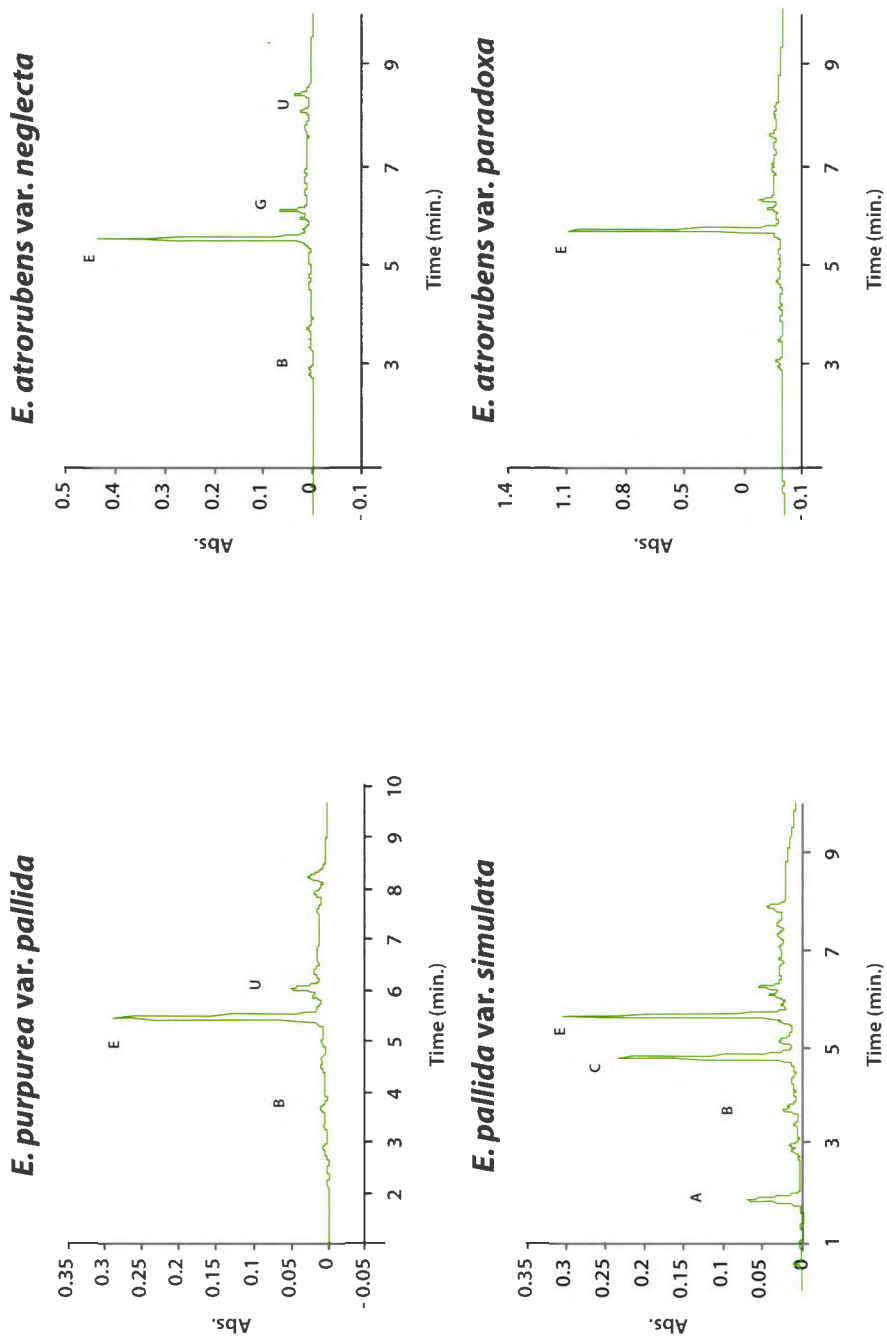


Figure 5. HPLC chromatograms of typical root profiles of hydrophilic phytochemicals in each *Echinacea* taxon. Peaks are as follows: (A) caftaric acid, (B) chlorogenic acid, (C) cichoric acid, (D) cynarin, (E) echinacoside, (F) cichoric acid methyl ester, (G) rutin, (H) caffeic acid, (U) unconfirmed (quinoyl), (UC) unconfirmed (di-caffeoyl). For compound structures see Figure 3. Absorbance was detected at 326 nm.

Diversity and rarity in natural populations of *Echinacea* species and the case for cultivation of this natural resource

Degradation in wild populations and increased rarity has been observed over the last few decades during the *Echinacea* boom. Publicly-acknowledged rare taxa (and the

states in the United States where they naturally grow, shown parenthetically) include:

E. laevigata (GA, MD, NC, PA, SC, VA) (USFWS, 2004: first listed 1982, recovery plan enacted in 1995)[18]

E. pallida var. *tennesseensis* (TN) (USFWS, 2004 first listed 1979, recovery plan enacted 1989)[18]

E. pallida var. *pallida* (MO)

E. pallida var. *simulata* (MO)

E. pallida var. *sanguinea* (LA, TX, OK)

E. atrorubens var. *paradoxa* (MO)

E. atrorubens var. *neglecta* (TX, OK)

Our taxonomic treatment of the genus did not lead directly to revision or clarification of protection laws regarding *Echinacea*. This is largely because while the taxonomic nomenclature changed, it has not yet been applied at the practical level of plant identification. Our assessments of diversity within genus *Echinacea* (genotypic and phenotypic) should be considered together with ecological evidence[26] in order to guide the taxonomic and practical protection of species and varieties that are at risk.

Ecophysiology, Competition, and Establishment

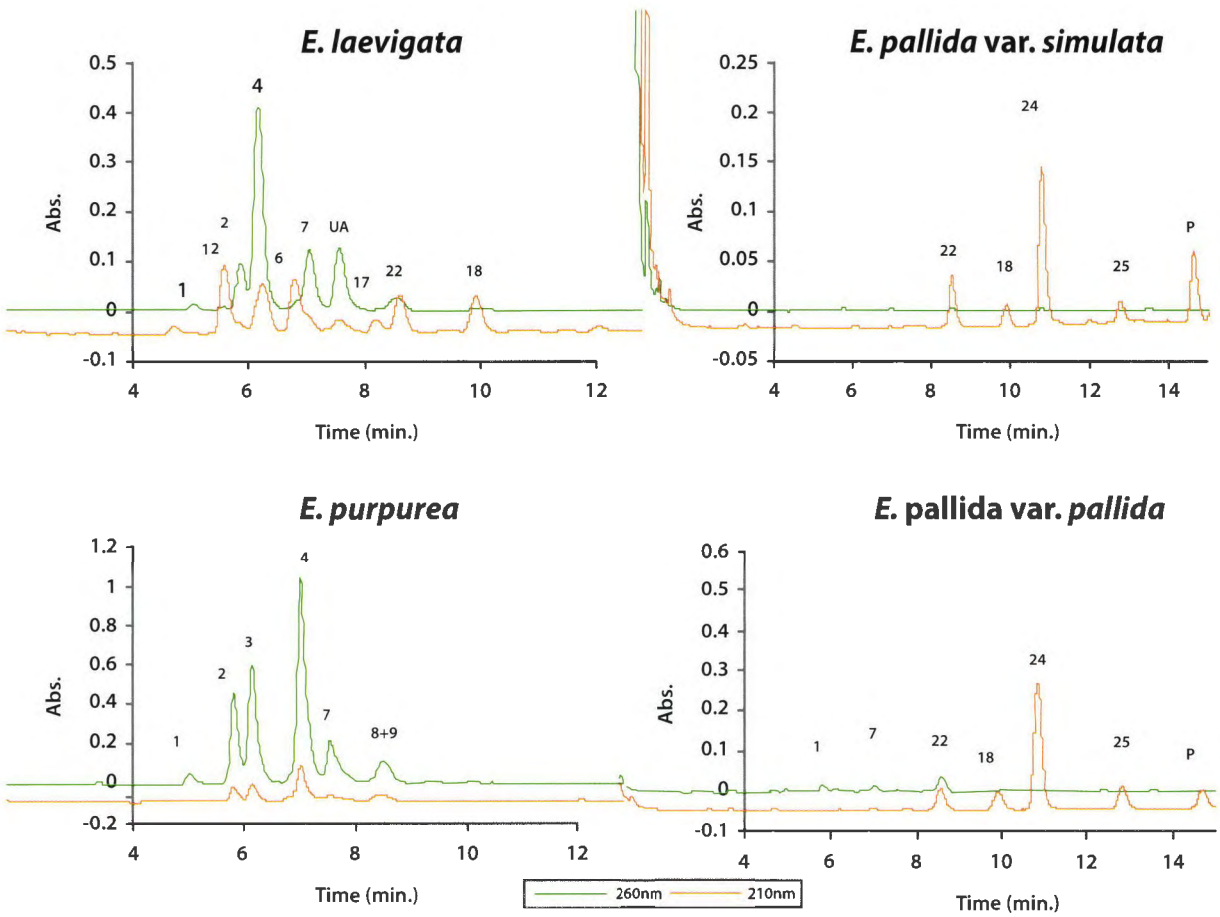
E. laevigata and *E. pallida* var. *tennesseensis* are located in marginal and highly vulnerable sites, on calcareous soils, in open woods, and in cedar barrens. It is likely that these and other "rare" taxa in this genus arose in Savannahs, which were caused and maintained by fires set by Native Americans.

In Tennessee, where *E. pallida* var. *tennesseensis* is the showy state wildflower, the ecological status and recovery of this *Echinacea* taxon has long been researched.[27,28,29,30,31] Recovery operations in place by US Fish and Wildlife, partnered with the State Department of Environment and Conservation, include the following measures: restriction of vehicular traffic, added fencing, limited livestock use of the areas (there is evidence that cattle graze on plant competitors and thus might increase seedling establishment and survivorship), public education projects, ecological monitoring, and acquisition of land by the Nature Conservancy, as well as by federal and state departments. Very rare populations will be deemed "recovered" when at least 5 populations are self-sustaining (i.e., stable or increasing over at least 10 years, with at least 2 juvenile plants for every adult plant). Through this rigorous recovery activity and monitoring, *E. pallida* var. *tennesseensis* is expected to be down-listed from "endangered" to "threatened" in January, 2007 (T. Merritt, Personal Communication, USFWS Cooksville, Tennessee, August 22, 2006).

Is rarity an ecophysiological occurrence?

It was found that *E. pallida* var. *tennesseensis* plants are not highly competitive compared with other glade species, especially under the effects of allelopathy [release of chemical substances by one species that inhibit the germination and/or growth of other species of plants] by species such as: *Juniperus virginiana* L., Cupressaceae, and *Dalea gattingeri* (Heller) Barneby, Fabaceae [syn. *Petalostemon gattingeri* Heller].[30,32] Moreover, plants of this variety do not have significantly different ecophysiological requirements in terms of their light and moisture use.[29]

Root physiology directly affects competitive abilities. *Echinacea* plants are taprooted forbs, which have difficulty establishing in both mixed and tallgrass prairie due to the competitive advantage of native grasses. However, *E. pallida* var. *angustifolia, Psoralidium tenuiflorum* (Pursch.) Rydb. Fabaceae (Slimflower scurfpea),



Dalea spp. L. Fabaceae (Prairie clover), and other taprooted forbs generally outperform rhizomatous forbs, which compete directly with grasses for nutrients.[33] Edaphic constraints [factors pertaining to soil ecological relationships] due to competition for nutrients and water are higher for rhizomatous forbs.[26]

There is also evidence that ecological variation (such as edaphic characteristics) affects genomic variability and/or expression of secondary chemistry. Chemotypes or chemical races were distinguished for populations of *E. pallida* var. *angustifolia* grown from wild seed,[5] despite widespread and mostly continuous distribution of *E. pallida* var. *angustifolia* in a range of habitats. On the other hand, a significantly lower genetic diversity was measured in *E. pallida* var. *tennesseensis*[17,27] and was attributed to possible historical extinction and colonization events.[27] These 2 taxa are distinct but closely related, since the genetic makeup of *E. pallida* var. *tennesseensis* is identical to that of *E. pallida* var. *angustifolia* at 50% of genes studied by isozyme analysis, and there appears to be a subset of var. *angustifolia* alleles at another 28% of *E. pallida* var. *tennesseensis* genes studied.[4,27]

Restoration of native prairie *Echinacea* populations is likely to depend largely on the other plants in the community. Seed recruitment is low. In some prairie remnants, there is evidence that wild-harvested *Echinacea pallida* var. *angustifolia* can resprout from holes where root fragments are left after digging (K. Kindscher, personal communication, June 5, 1999); however, the degree to which it may compete for establishment is still under

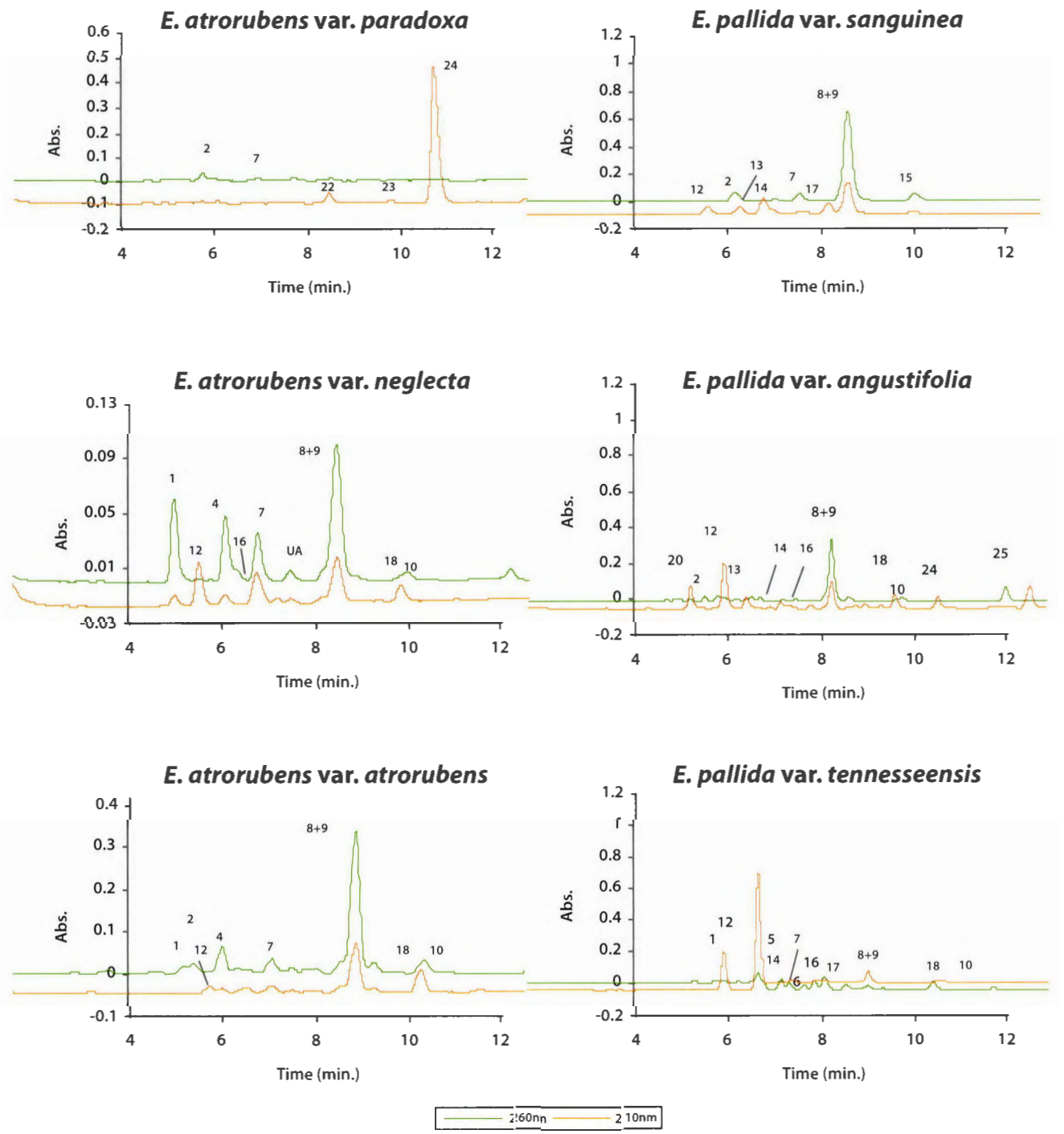


Figure 6. HPLC chromatograms of typical flowerhead profiles of lipophilic phytochemicals in each *Echinacea* taxon. Numbered peaks correspond to Figure 4. Lettered peaks are as follows: (P) unreported polyene that resembles 22 by UV-scan, (*P) unreported polyene (UV-scan identical to 24), (UA) unreported diene alkamide, (UA*) unreported tetraene alkamide.

longer-term study.

E. purpurea has been used for comparisons of competitive abilities (plant size and reproductive capacity) between wild and cultivated populations. Snyder *et al* showed that wild plants tend to have increased vegetative growth, while cultivated plants display increased reproductive capacity.[34]

Is rarity a result of human activity?

Wilcove *et al* implicated habitat degradation in the decline of 85% of 1880 species of imperiled plants and animals in the United States.[35] Thirty-five percent of these were directly linked to commercial and residential human developments. Road construction and maintenance were almost equal. However, in the case of *Echinacea*, the largest human influence on rarity in certain taxa is undoubtedly wild-harvesting for the herb/dietary supplement trade.

Echinacea harvesting is controversial and, likely due to mass commercialization of the 1990s, it was particularly rampant throughout the Native American Indian reservations across the Great Plains. In 1990, North Dakotan people were encouraged to "just grab a shovel and start digging" while "environmentalists in the state fear[ed] that gold fever [was] spreading among shovel wielding collectors with dollar signs in their eyes."[36] "Rooting," as the digging of *E. pallida* var. *angustifolia* roots was called, has been an economic opportunity for both native and non-native people, as well as an ethical wildcrafting nightmare—where poachers have been known to effectively clear out wild populations of the plants without concern for preservation of the resources or the ecosystems.[37]

Early regulation of the rampant wild harvesting came in the form of tribal resolutions in several states and later as legislation. For example, by 1999 North Dakota began to fine poachers $10,000 along with confiscation of their vehicles.[37] In Montana, a 3-year moratorium on the harvest of *E. angustifolia* from state lands, pushed by herbalist R. Klein,[37] led to the current Montana Code, which prohibits wild harvesting of *E. pallida* var. *angustifolia* from public lands without a permit, with a fine up to $1000 or 6 months in jail.[38] Despite these efforts, permits are still issued to dig for personal use (not commercial sale) of *E. pallida* var. *angustifolia* roots in Montana, and the harvesting regulation does not apply to aboriginal reservations or private landowners. Clearly, *Echinacea* prairie varieties at risk from ecophysiological factors and issues of genetic constraints, as discussed previously, have also been under risk of human mismanagement.

Public land conservation is achieved through scientific input provided to land management agencies and lobbying for federal legislation.[39] Conservation and restoration on private lands was traditionally achieved through zoning, condemnation, and tax regulation, with little success. Innovative bottom-up approaches are increasingly addressing private land degradation and slowing or halting the ravaging of natural ecological communities. Land trusts, open-space tax incentives, "community-based conservation," and more have begun to effectuate stewardship. The Plant Conservation Alliance, which formed its "Medicinal Plant Working Group" in 1999, has established links between the Nature Conservancy and other institutions, NGOs, and the public in a "bottom up" effort to change wild harvesting practices. In fact, *E. pallida* var. *pallida* and *E. pallida* var. *angustifolia* were cited on the list of "Medicinal Plant Species in U.S. Commerce" as top priority warranting further study; the authors based their assessment on 1989-1999 data for trade demand increases, wild population declines, and species decline.[40] Finally, government grants ($3 US million in 2004) are now being awarded to protect plant species on tribal lands.[41]

Echinacea purpurea Photo ©2006 stevenfoster.com

Echinacea pallida Photo ©2006 stevenfoster.com

Echinacea angustifolia Photo ©2006 stevenfoster.com

Echinacea sanguinea Photo©2006 Tom Barnes, University of Kentucky.

Take-Home Messages

Echinacea forbs compete poorly to fairly with native grasses in prairie sites, resulting in low recruitment of *Echinacea* by seed. Significant factors include the following:

Public lands are relatively easy to protect with scientific evidence (data exist).

Private lands require new model for community-based natural resource management.

Habitat degradation due to development and human activity is the primary cause of rarity.

Echinacea wildcrafting is not sustainable.

Conclusion

During the herbal renaissance of the 1990s, *Echinacea* plants were the subject of much interest, common usage, and research scrutiny. Now, as science and markets for medicinal plants continue to evolve in the 21st century, the integration of findings from state-of-the-art original morphological, molecular, and phytochemical work by the authors of this article, along with ecological reports and the historical and regulatory literature of the times, suggests that these North American native plants deserve their status as protected resources. Moreover, it provides a comprehensive perspective into the biological and political origins of *Echinacea* materials sourced as phytomedicines, which is long overdue considering the focus on clinical evidence for *Echinacea* health products and dietary supplements. HG

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Medicinal Plants of Montenegro

by Steven Foster

When I arrived in the capital of Podgorica (pronounced pod-gor-EE-za), on May 22, 2006, thousands of red Montenegrin flags adorned with the double-headed eagle flew from balconies, cars, and in the hands of people in the streets. The day before, by popular vote under the watchful eye of European Union observers, Montenegrins voted to secede from the Union of Serbia-Montenegro, also known as the Federation of Yugoslav Republics. After nearly a century, Montenegro is once again an independent democratic country. Europe's newest independent country is small in size, big in heart, with a diverse and spectacular natural beauty rivaled by few countries of comparable size. In 1991 the Montenegrin Assembly was the first state entity to declare itself an "ecological state."

Ask most Americans where Montenegro is and they may respond with a question — "An island in the Caribbean?" No. The Italian moniker "monte negro" (black mountains) was bestowed by passing seafarers along the Adriatic Coast, due to the dark forests that once covered the Dinaric Alps as seen from the Adriatic. The name Montenegro, or *Crna Gora* as it is known in the local Serbian dialect, has stuck for more than 500 years. Montenegro is a tiny country, barely the size of Connecticut with a population of fewer than 700,000 souls. It lies on the mid-Adriatic coast, with Albania to the South, Croatia and Bosnia and Herzegovina to the north, and Serbia and Kosovo on its eastern borders.

Montenegro has always existed on the periphery of attention. For centuries larger neighbors overshadowed this country, one of the oldest in the world. Post Neolithic settlement began in the 6th century BCE with the establishment of Illyrian coastal towns. Fifty miles inland on the Zeta Plain, the ruins of the ancient Roman outpost of Doclea (Dukllja) are minutes from downtown Podgorica, the modern capital. The Romans established Doclea in the first decade of the first century as an ancient caravan route once linking Albania and Croatian cities at the confluence of the Morace and Zeta rivers. Following the decline of the Roman Empire, Avars and Huns filtered into the region under the nominal rule of Constantinople (present day Istanbul), the capital of the Byzantine Empire. By the seventh century, Slavs from the Baltics and Poland made their way to the Adriatic, and the Slavic state of Zeta emerged.[1] Zeta, which means "the harvesters," recognizes the long history of wild harvest of foods such as pomegranates and figs along the coast, plus medicinal plants, aromatic herbs, and wild mushrooms in the spectacular mountains of modern Montenegro.[2]

Mountain field of St. John's wort *Hypericum perforatum*. Photo ©2006 stevenfoster.com

The flora of Montenegro is one of the most diverse of any comparable-sized temperate or subtropical region in the world. Montenegro is located in the southwest part of the Balkans, encompassing an area of 13,812 km^2 (5,331 sq. miles) and is not more than 173 km (107 miles) from east to west, with a 316 km (196 mile) long coastline along the Adriatic. The country is mostly mountainous, with only 10% of its land area below 200 m (656 ft.) in height. Montenegro is generally classified as having a Mediterranean climate along the coast and continental climate inland, though microclimates can be found along the coast, valleys, mountains, and plateaus, creating a diversity of habitats with subtropical to alpine floras. The geological features form 3 distinct floristic zones, including the inland mountains, the central lowland plain, and the Adriatic coast. The diverse climate and relief features create a high degree of biological diversity in a very small territory.[3]

Montenegro has 3,136 vascular plants, of which 659 species are medicinal. In the coastal region approximately 174 species have recognized medicinal value. In the central highlands, as many as 540 medicinal plant species are found, and in the Balkans to the north, at least 479 species can be documented as medicinal plants. According to Dragan Dragojevic, PhD, CEO of Aroma Sp. Dragojevic, an essential oil producer, there are 133 pharmacopeial species in Montenegro. Dragojevic's 1987 PhD dissertation from a university in Macedonia was on medicinal plants of Montenegro. Three of the top 15 best-selling herbs on world markets are wild-harvested in Montenegro, including St. John's wort (*Hypericum perforatum* L., Clusiaceae), valerian (*Valeriana officinalis* L., Valerianaceae), and bilberry (*Vaccinium myrtillus* L., Ericaceae). In addition, the Adriatic coast from Albania to Montenegro is the world's largest production region of wild-harvested Dalmatian sage (*Salvia officinalis* L., Lamiaceae).

The coastline along Montenegro's western boundary is the eastern side of the Adriatic; buffered by sea currents and winds, this coastline is warmer and clearer than the Italian side on opposite shores. There are at least 7 ancient cities, each one a former capital of smaller kingdoms, protectorates, and vassals of Slavic, Ottoman, and Venetian empires: Ulcinj, Bar (famous for olive oil production), Budva, Tivat, Risen, Herceg Novi, and the walled medieval city of Kotor tucked beneath St. John's Mountain at the end of Boka Kotorska (Bay of Kotor). Kotor is a UNESCO World Heritage Site.[4] All along the coast, small villages, like the fishing village island turned hotel, Sveti Stefan, abound with charm and Mediterranean herbs.

The coastal hinterlands dip into a rugged, yet friendly coastline, with mountains holding a flora typical of Mediterranean climates. Familiar herbs in the mint family (Lamiaceae or Labiatae), such as winter savory (*Satureja montana* L.), sage (*S. officinalis* L.), thyme (*Thymus* spp.), and oregano (*Origanum vulgare* L.), abound in the dry rocky soils, under the shadow of the spires of Italian cypress (*Cupressus sempervirens* L., Cupressaceae), basking beneath the hot Mediterranean sun. Here thickets of wild figs (*Ficus carica* L., Moraceae), chaste tree (*Vitex agnus-castus* L., Verbenaceae), wild pomegranate (*Punica granatum* L., Punicaceae), and Scotch broom (*Cytisus scoparius* [L.] Link, Fabaceae) surround ancient olive groves on mountain slopes that dip into the turquoise waters of the Adriatic below.[5]

Dalmatia, from the Island of Rab in northwest Croatia to the Gulf of Kotor in Montenegro, is the origin for much of the world's common garden sage (*S. officinalis*), "Dalmatian Sage"—the familiar culinary herb and phytomedicine. More than 50% of the world's supply is still wild-harvested along the Adriatic coast from Albania in the south to the Croatian coastal mountains north of Montenegro. In 2005, the US imported 2,007 metric tons of sage leaf from Albania, 1.5 tons from Bosnia and Herzegovina, 244.7 tons from Croatia, and 54 tons from Macedonia. The last reported US imports of sage from Serbia and Montenegro was in 2003. However, a portion of the tonnage exported from Albania, Bosnia and Herzegovina, and Croatia was wild-harvested in Montenegro and sold to buyers in neighboring countries.[6] As an understory subshrub, sage is a dominant floristic element in the coastal mountains, with its azure blue flowers covering the dry rocky landscape. This is the center of diversity for this common culinary herb. Variations have been recognized in somewhat archaic botanical subspecies, varieties, and forms including such designations as *S. officinalis* L. f *pallida* Pant. with white flowers, *S. officinalis* subsp. *officinalis* var. *officinalis* f. *brevipedicellata* Gajic, *S. officinalis* subsp. *officinalis* var. *officinalis* f. *bracteata* Gajic, and *S. officinalis* subsp. *officinalis* var. *officinalis* f. *longiaristata* Gajic, among others.[7]

Gentian *Gentiana lutea* **on Mt. Sinjavina. Photo ©2006 stevenfoster.com**

Montenegro, prior to the break-up of the former Yugoslavia, was an important and vibrant trading center for medicinal and aromatic plants, primarily wild-harvested in the Balkans and the Coastal Mountains. After the Balkan civil wars began in the early 1990s, Montenegro, then still a state within Serbia, suffered from United Nation sanctions and later from NATO bombing. This halted exports of bulk medicinal and aromatic herbs from Montenegro, which at that time had an export business approaching $50 (USD) million a year in sales. The period of sanctions devastated the herb sector. Sage sales plummeted and much of the bulk business shifted to Albania. Today, Montenegro is in the process of rebuilding, with container loads of sage once again being shipped to international destinations.

Above: **Oregano** *Origanum vulgare* is a common wild herb. Photo ©2006 stevenfoster.com
Right: Woman in traditional garb harvesting bilberries *Vaccinium myrtillus*. Photo ©2006 stevenfoster.com

The distinct silver gray leaves of olive (*Olea europea* L., Oleaceae), now valued for their antioxidant and antihypertensive activity, are a familiar site along the coastal region. Bar, a small port city located on the Adriatic coast in southeastern Montenegro, has a mild Mediterranean climate, buffered by the warm current of the Adriatic, and tempered by Skadar Lake, with Mountain Rumija massif between. This ancient city has been inhabited since Neolithic times. Ancient Illyrian, Greek, and Roman cultures all inhabited the area. By the 7th century it was populated by the Slavs. Among the nearly 500,000 olive trees in ancient groves along the Montenegro coast is a special treat for those who make their way to the village of Mirovica just north of Bar, where a local park protects a 2000-year-old olive tree—one of the oldest in the world. Legend holds that before marrying, men must plant 10 olive trees, which resulted in nearly 500,000 olive trees growing today in ancient groves along the Montenegrin Coast. Bar has once again become an important olive oil production region as the result of a United States Agency for International Development (USAID) program that has helped to reclaim once-abandoned olive groves.

Throughout Montenegro, St. John's wort commonly blooms from late May to August, depending upon the region and the elevation. Traveling along the Montenegrin coast in July and August, one may come across an occasional vendor selling bottles of *Kanatrionovo Ulje*—St John's wort oil. Under the hot Mediterranean sun, in much the same way that it has been for centuries, the red-colored oil made from the yellow flowers is used to treat first-degree burns, along with bruises and other skin conditions. Once known to pharmacists as "red oil" or "Hypericum liniment," it is still available in European pharmacies. In Montenegro, the oil is sold along the coast as a kind of "tanning oil" to create a dark tan, though in light-skinned individuals this practice could cause an unpleasant dermatitis.*

In late June, heading inland toward the Zeta Plain over Mt. Lovcen or Mt. Rumija toward Skadar, the largest inland lake in the Balkans, a dominant flowering plant is *Helichrysum italicum* (Roth) G. Don, Asteraceae. The flowering tops are collected by villagers along the coastal mountains and the Skadar Lake region and sold to buyers for distillation of the essential oil. Known regionally as immortelle, or in the American nursery trade as "curry plant," the essential oil has been shown to have significant antibacterial activity[8] as well as anti-inflammatory and antioxidant activity.[9] Aromatherapists use the essential oil to facilitate the healing of wounds and scars. One of the reasons it has not gained more popularity is its great expense compared with other essential oils.

Driving north toward the Mt. Sinjavina massif, one transitions from a Mediterranean flora to a continental flora and high alpine slopes, some over 2,500 meters tall with familiar medicinal plants typical of Central Europe, such as linden (known in some areas by the common name "lime tree," *Tilia* spp., Tiliaceae), bilberry, and gentian (*Gentiana lutea* L., Gentianaceae). Climbing the steep truck-choked main highway up

* This condition, called "hypericism," was first recorded in 1787. When light-skinned livestock, such as sheep, goats, horses, and cattle ingest the plant, and then are exposed to bright sunlight, they may develop welts on the skin, and other symptoms. Dark-skinned animals are largely unaffected. This photodermatitis is the result of the interaction of sunlight and oxygen with the pigment hypericin. After being ingested, it is absorbed though the intestinal wall and reaches the blood without being eliminated by the liver or kidneys. Photosensitization generally does not occur, and has not been recorded from external contact with the plant. Source: Kingsbury *J. Poisonous Plants of the United States and Canada*. New Jersey: Englewood Cliffs; 1964:173.

Above and Left: **Wild sage** *Salvia officinalis* is common on Mt. Rumija. Photos ©2006 stevenfoster.com

Mt. Sinjavina, one reaches a continental divide where water flows westward toward the Adriatic on the western slope, and toward the Black Sea from the eastern slopes. This eastern slope holds the headwaters of the Tara River valley, creating a spectacular deep canyon, second only in length to the Grand Canyon. The azure blue waters, considered the cleanest in Europe, cut through Beograd Gora National Park toward the Mt. Durmitor massif, the tallest mountain group, with 49 peaks over 2,000 meters atop a vast plateau 1,500 meters above sea level, and intersected by deep canyon gorges and 18 pristine glacial lakes. Here in calcareous soils of the high mountain glades and plateaus of Montenegro is the home of yellow gentian (*G. lutea* spp. *symphandra* [Murb.] Hayek), the root of which has long been valued as a bitter tonic. Yellow gentian is one important medicinal plant which has become threatened in Montenegro and throughout its range due to factors ranging from relative scarcity in a limited high mountain habitat to over-harvest. The export of the root is now banned from Montenegro. According to Donnelly and Helberg, the status of *G. lutea* in Serbia and Montenegro is vulnerable, its legal status is protected, and the supply used there is from imported sources.[10]

Today former traders in gentian root are keenly interested in its conservation. Mr. Veselin Vucinic is one such person. He is the owner of Flores, an herb tea, bulk herb, and essential oil producer in Mojkovac, located just down river from the Tara River Canyon. He formerly purchased upwards of 60,000 kg of gentian root before its harvest was banned. Mr. Vucinic no longer trades the dried root, but he is keenly interested in the species' long-term sustainability.

On Mount Sinjavina in the central high mountains and plateau region of Montenegro, *G. lutea* populations seem to be increasing. For the past 5 years, Mr. Vucinic has been encouraging villagers in remote mountain hamlets and seasonal shepherds to be more aware of the plant's future. Here there are no tractors, mowing machines, and hay balers. Hay is cut by hand with a scythe, then raked by hand and neatly piled into haystacks. When Mr. Vucinic is traveling in the mountains buying common herbs, he often sees farmers cutting hay. He stops and politely asks that they not cut flowering and/or fruiting *G. lutea* plants, and he encourages them to let the plants go to seed. This informal conservation effort serves to help increase awareness of the plant and its sustainable development for the future. This regeneration effort is an excellent model for the development of sustainable supplies of this threatened species and Mr. Vucinic should be commended for these efforts. Attention to simple conservation measures, such as this, has resulted in an increase in gentian, where it had once disappeared.

Further north and east toward the Serbian and Kosovo borders, each year in the city of Plav in northeastern Montenegro, a beautiful mountain city overlooking the placid waters of Plav Lake, the annual Bilberry Festival is held, celebrating the harvest season of this native wild fruit. "Blueberry," as it's known locally in Montenegro, is traded in world markets as "bilberry" (*Vaccinium myrtillus* L., Ericaceae). Bilberry jam and

juice products are widely available in markets in Montenegro. Since imposition of UN sanctions on the former Yugoslavia in the early 1990s, the bilberry harvest has fallen to less than half of its former tonnage of 600 metric tons of fresh berries. Seven years ago in an effort to redevelop this wild-harvested crop, the regional government for Plav and business concerns began the annual Bilberry Festival. This year's harvest is estimated at 200 metric tons.

Wild thyme *Thymus* spp. is known as "mother spirit." Photo ©2006 stevenfoster.com

During the filming of a remake of a Tarzan movie in the early 1970s, the starring Danish actress, Kitty Swan, fell into a fire on the movie set and was severely burned. For treatment she turned to the Montenegrin herbalist J. Saljic, whose family has included practicing medical herbalists in the central mountain city of Berane for over 300 years. Saljic became famous for a special herbal treatment for burns. Today, one of Saljic's sons, Bozidar-Bosko Saljic, along with his son, Petar Saljic, carries on the tradition, both clinically and commercially, manufacturing as the MN&Saljic Company in Podgorica. The family runs a clinic where individuals with various dermatological problems ranging from severe acne to burns are treated with herb products manufactured by the company. These products are available in every pharmacy in Serbia and Montenegro, but not known outside their borders. In addition, cosmetics, burn ointments, and salves, as well as custom-blended herbal tea preparations, are shipped to individual clients throughout the world. The ingredients are all wild-harvested from mountain ranges with Ecocert® wild organic certification. Unknown herbal treasures like those held by the 300-year-old tradition of the Saljic family are yet another herbal resource of Montenegro.

Montenegro's tradition of harvesting wild medicinal herbs dates back centuries, if not millennia. Relative geographic and political isolation have hidden this fact outside of the Balkans until now. "Montenegro has huge potential thanks to its climate—Mediterranean as well as continental," says Bozidar-Bosko Saljic. "In such a small area we have among the world's richest and well-developed herbal traditions." HG

Author, photographer, and consultant, Steven Foster is co-author (with Rebecca Johnson) of the recently published National Geographic book Desk Reference to Nature's Medicine, *2006, National Geographic Society, Washington, DC.*

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Appeals Court Sides with FDA in Ephedra Ban Case

by Madeline Hollern and Courtney Cavaliere

A three-judge panel of the 10th Circuit US Court of Appeals ruled in favor of the US Food and Drug Administration (FDA) on August 17, 2006, in a case that had challenged the FDA's 2004 complete ban of ephedrine alkaloids in dietary supplements.[1]

The Nutraceutical Corporation and its brand Solaray® brought a legal challenge against the FDA in May 2004, a month after an FDA regulation banning ephedrine alkaloids at any level from dietary supplements went into effect.[2,3] Prior to that regulation, extracts of ephedra (*Ephedra sincica* Stapf, Ephedraceae) were common ingredients of numerous weight-loss products, including a dietary supplement produced and marketed by Solaray.[2] Nutraceutical challenged both the FDA's use of a risk/benefit analysis in determining an "unreasonable risk" of ephedra, as well as the regulation's ban on low dose ephedra products. Solaray's dietary supplement was marketed as delivering less than 10 mg per day of ephedrine alkaloids. The US District Court for the District of Utah ruled in favor of Nutraceutical on both of these causes of action in April 2005,[4] and these rulings have now been overturned by the Court of Appeals.

Nutraceutical Corporation's counsel Jonathan Emord criticized the court's decision (e-mail to C. Cavaliere, September 5, 2006). "If the 10th Circuit decision remains unchanged, it bodes ill for the entire industry. It stands for the proposition that the new drug risk (safety)—benefit (efficacy) comparison may be adopted by FDA in the Food Adulteration context. That move is unprecedented and enables FDA to avoid the more rigorous precedent that has since the turn of the twentieth century compelled FDA to prove a risk of illness or injury under conditions of actual use, rather than on general pharmacologic principles and in reliance on hypothetical models."

According to Emord, FDA had no direct evidence that supplements containing low doses of ephedrine alkaloids presented any risk of illness or injury, and FDA officials instead paid an expert to extrapolate data from studies concerning the effects of the drugs epinephrine and isolated ephedrine and apply them to the context of supplements containing ephedrine alkaloids. "Never before in the history of the Food Adulteration provision had FDA been allowed by a federal court the discretion to ban a dietary supplement outright based on indirect evidence and no establishment of a precise dose at which toxicity arises," Emord wrote.

The FDA's use of a risk-benefit assessment against ephedra also shows that the agency can strengthen its case against a product by declaring the product's benefits as non-significant. For instance, FDA did not consider weight loss a significant benefit of ephedra. "FDA refused, in its rulemaking process, to acknowledge any benefits for ephedra, even for traditional uses," stated Michael McGuffin, president of the American Herbal Products Association.[2] "If the benefit side is judged as 'zero,' the outcome of any risk/benefit analysis will necessarily be skewed. But this court has now specifically stated that FDA's risk/benefit mechanism 'correctly followed the congressional directive,' and industry will need to evaluate the implications of this as precedent."

According to Emord, Nutraceutical intended to file a petition for rehearing in front of the entire 10th Circuit Court of Appeals at the end of September. If denied, the company will take its case to the Supreme Court. "To be sure, it is never easy to defeat the FDA, but if the rule of law is to have true meaning, and if the will of Congress and the rights of the regulated class are to be respected, we have no choice but to defeat the FDA," wrote Emord.

The 2004 ban of ephedra, which attracted much media attention, was the first time the FDA had removed a popular dietary supplement from the market under the provisions of the Dietary Supplement Health and Education Act (DSHEA) of 1994.[5] The FDA ban was largely inspired by the high profile deaths of several sports figures who used the supplement, and it was preceded by ephedra bans within certain states and by various sports organizations. Nutraceutical earlier explained that its lawsuit against FDA was not filed in an attempt to reinstate sales of ephedra supplements but to deter arbitrary rules by the FDA that could cause problems for the entire supplement industry.[6] The District Court of Utah's 2005 ruling in favor of Nutraceutical found fault with the FDA's use of a risk-benefit analysis and the fact that FDA did not first prove the dosage at which ephedra presented an unreasonable risk.[4] That court's decision only lifted the ban on low-dose ephedra products and did not have any effect in certain states. FDA recently released an updated warning against ephedra through its safety information and adverse event reporting program MedWatch, declaring it illegal to market dietary supplements with ephedrine alkaloids at any dosage and stating that such products "are considered adulterated and pose an unreasonable risk of illness or injury to users, especially those suffering from heart disease and high blood pressure."[7] HG

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European Health Agencies Recommend Liver Warnings on Black Cohosh Products

ABC, Herb Experts, and NIH Workshop Find No Direct Causal Relationship between Popular Menopause Remedy and Rare Reports of Liver Problems

by Mark Blumenthal

Two European health agencies have published warnings for possible liver toxicity for black cohosh products. The United Kingdom's Medicines and Healthcare products Regulatory Agency (MHRA) announced on July 18, 2006, that warnings will be required on labels of all black cohosh (*Actaea racemosa* L., Ranunculaceae; syn: *Cimicifuga racemosa* [L.] Nutt.) products, due to concerns about a suspected association between black cohosh and risk of liver disorders.[1] MHRA, the UK government agency responsible for ensuring the safety of medicines and medical devices, based its decision on the conclusions of the Commission on Human Medicines and the Herbal Medicines Advisory Committee, both of which claimed to have reviewed all available data on the subject and found what they have determined to be a possible association between black cohosh and increased risk of liver disorders. However, at this time there is no scientific evidence in the published pharmacological and toxicological literature supporting this alleged connection with hepatotoxicity. In fact, various black cohosh preparations have shown high levels of safety in numerous clinical trials and widespread, long-term use.

The European Medicines Agency (EMEA) released a press statement on July 18, 2006, urging patients to stop taking black cohosh if they develop signs suggestive of liver injury (i.e., tiredness, loss of appetite, yellowing of the skin and eyes, or severe upper stomach pain with nausea and vomiting or dark urine) and advising healthcare professionals to ask patients about their use of black cohosh products.[2] The EMEA's Committee on Herbal Medicinal Products (HMPC) evaluated 42 case reports of hepatotoxicity. Although the vast majority of cases were found to be insufficiently documented or otherwise inappropriate for an analysis, the HMPC ultimately concluded that there is a potential connection between herbal medicinal products containing black cohosh root and hepatotoxicity.[2] The EMEA policy guidance is to be enforced on a country-by-country basis.

Black Cohosh *Actaea racemosa*. Photo ©2006 stevenfoster.com

Philip Routledge, chair of the UK Herbal Medicines Advisory Committee, was quoted in a press release from the UK MHRA as saying that, "After reviewing all available data, the Herbal Medicines Advisory Committee has come to the conclusion that black cohosh may be associated with liver disorders. This is rare, but can be serious."[1]

Kent Woods, MHRA's chief executive, was quoted in the same press release, saying, "In the light of this advice, the MHRA is working with the herbal sector to ensure that labels of black cohosh products carry updated safety warnings. The labels will point out the possible symptoms so that appropriate action can be taken without delay."[1]

The proposed wording for UK products is reported as follows: "Warning: In rare cases, black cohosh may cause liver problems. Consult your doctor if you already have liver disease or become unwell whilst using this product."[3]

In August, Health Canada issued a public warning on the potential association of black cohosh and liver toxicity but did not go so far as to propose a warning for product labels.[4] (See sidebar)

The German government is reportedly conducting an extensive review of black cohosh safety, particularly with respect to the liver-related adverse event reports (Mahady G., personal communication, Sept., 25, 2006).

To date, there is no published scientific evidence supporting the suggestion that black cohosh may have an adverse effect on liver function. While the available adverse event reporting data indicate a possible association between black cohosh and liver disorders in a relatively few rare cases, regulators, clinicians and scientists generally agree that well documented clinical and scientific data are lacking to prove a causal relationship. Black cohosh has

had a strong history of safe use by millions of women in Europe, the United States, and in other regions, and many controlled clinical trials support the safety and efficacy of black cohosh preparations in treating menopausal symptoms.

Professor Norman R. Farnsworth, PhD, research professor of pharmacognosy and director of the Program for Collaborative Research in the Pharmaceutical Sciences at the University of Illinois at Chicago (UIC), is currently conducting clinical research on a black cohosh extract under a long-term grant from the National Institutes of Health (NIH) National Center for Complementary and Alternative Medicine (NCCAM). He and his colleagues have conducted a virtually exhaustive review of the pharmacological, toxicological, and clinical literature on black cohosh. "In our black cohosh clinical trials that we have been conducting, in which we have been monitoring liver enzymes in all women enrolled, we have observed no increases in enzyme levels over the one-year trial period," said Dr. Farnsworth (personal communication, July 20, 2006). Dr. Farnsworth, an internationally recognized herb expert, does not believe that there is adequate scientific or clinical data available upon which to make regulatory policy on black cohosh. (Dr. Farnsworth is a founding member of ABC's Board of Trustees.)

Professor Edzard Ernst, MD, director of complementary medicine at the Peninsula Medical School, Universities of Exeter & Plymouth in the UK, and an internationally recognized authority on the medical literature of herbs and phytomedicines, stated that only 4 of the case studies reviewed by the MHRA are adequately documented to the extent that any meaningful inferences can be drawn from them. "I understand that regulators have to err on the safe side, but I wonder whether this is not some overreaction as black cohosh has been used for a long time," said Ernst.[3] Supporting the same position taken by Dr. Farnsworth, Dr. Ernst said he was not aware of any scientific or clinical research

Health Canada Issues Advisory on Black Cohosh

Health Canada recently issued an advisory about a possible link between products containing black cohosh (*Actaea racemosa* L., Ranunculaceae; syn. *Cimicifuga racemosa*) and liver damage.[1] The advisory, issued August 18, 2006, does not address the issue of whether black cohosh products should have warnings on their labels because that is dealt with during the licensing review required of all herbal products to be sold legally in Canada. The advisory cites 3 case reports of liver damage in Canada that may have been associated with black cohosh and follows similar advisories and warnings about black cohosh recently adopted by other health agencies in the UK and Australia.

In its advisory, Health Canada encourages consumers to exercise caution in the use of products containing black cohosh and to consult a healthcare practitioner with any concerns regarding its use.[1] The agency further advises consumers to discontinue use of black cohosh products and consult a physician if they exhibit unusual fatigue, weakness, loss of appetite, yellowing of the skin or whites of the eyes, dark urine, or abdominal pain. The advisory stressed that case reports of liver damage are rare and that most cases have involved contributing factors that may have led to or encouraged the liver damage. According to the advisory, Health Canada is currently reviewing the safety and effectiveness of black cohosh.

Robin Marles, PhD, director of the Bureau of Clinical Trials and Health Science at the Natural Health Products Directorate of Health Canada, explained that all 3 of the Canadian cases of liver damage supposedly associated with black cohosh had serious confounding factors, including patients' use of multiple prescription drugs in 2 of the cases and a prescription drug with alcohol use in the third. Dr. Marles said Health Canada purposefully included information in its advisory about such confounding factors and the fact that "the quality of the black cohosh products involved in these cases is not known," which other agencies were not as careful to do. Dr. Marles indicated that while any medicine may cause a very rare idiosyncratic adverse reaction, in most cases the problem is probably not due to authentic black cohosh but due to quality issues such as the identity and purity of the herbal material in products labeled as black cohosh (R. Marles e-mail to M. Blumenthal, September 8, 2006). This is in agreement with the opinions of world experts such as Professors Norman R. Farnsworth, PhD, of the University of Illinois at Chicago (a Trustee of the American Botanical Council), Edzard Ernst, MD, of the University of Exeter, UK, and Fredi Kronenberg, PhD, of Columbia University (also an ABC Trustee).

"It is common for some people to overreact to these cases and not see them in the light of alternatives such as hormone replacement therapy, which has a much higher rate of adverse reactions, or to compare liver toxicity of acetaminophen to black cohosh," wrote Dr. Marles in an e-mail to Dr. Kronenberg, a leading researcher on herbal remedies and women's health issues and director of the Rosenthal Center for Complementary and Alternative Medicine at the Columbia University College of Physicians and Surgeons in New York (e-mail, August 24, 2006).

"The advisory we issued is a compromise between the scientific facts and the need for regulators to take a precautionary approach to protecting the health of consumers. Hopefully the message will not cause undue alarm and our regulatory review will ensure that consumers continue to have ready access to high quality black cohosh health products," Dr. Marles added. HG

—Courtney Cavaliere

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demonstrating a hepatic mechanism of action for black cohosh (E. Ernst, personal communication, July 20, 2006).

Australia became the first country to require a warning on labels of black cohosh products earlier this year. An article in *HerbalGram* 71 described the Australian Therapeutic Goods Administration's (TGA) decision to provide warnings on black cohosh products, which was based on TGA's concerns about the potential association with liver problems.[5] The TGA policy requires the following label statement on black cohosh products: "Warning: Black cohosh may harm the liver in some individuals. Use under the supervision of a healthcare professional."[6] In establishing this policy, TGA acknowledged that some reports of adverse events have been confounded by multiple ingredients, more than one medication, or by other medical conditions, and that the incidence of liver reaction appears to be very low considering the widespread use of black cohosh. (A TGA official initially agreed to provide an explanation of the criteria and process used in TGA's decision-making, but has not responded to repeated requests from ABC for such clarification.)

The Swedish government has reportedly been recommending a liver warning on product inserts in black cohosh products for several years; however, according to a spokesperson, regulators do not plan to require a warning on the outside of such black cohosh packages.[3]

The US NIH held a 1-day Workshop on the Safety of Black Cohosh in Clinical Studies in November 2004.[7] The consensus of the experts assembled at the NIH conference concluded that there is inadequate evidence that black cohosh preparations are causally associated with hepatotoxicity. However, the workshop participants concluded that liver enzyme levels should be monitored in all women enrolled in NIH-funded trials on black cohosh, as a precautionary measure (as is being done by Professor Farnsworth's group at UIC).

In June of 2005, Schaper & Brummer, the German manufacturer of Remifemin, the world's most clinically researched and top-selling black cohosh preparation, introduced into the United States market new packaging with the following warning: "Consult your healthcare practitioner prior to use if you have a history of liver disease or are taking prescription drugs."[5]

Numerous published, controlled clinical trials support the use of several leading black cohosh preparations for reducing symptoms associated with menopause. Black cohosh has become one of the most popular herbal dietary supplements in the United States, ranked eighth of all single-herb supplements sold in mainstream retail outlets in 2005, according to data from Information Resources in Chicago as reported in *HerbalGram* 71.[8] HG

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UK Expert Committee Upholds Kava Ban

by Courtney Cavaliere and Mark Blumenthal

The United Kingdom's Committee on Safety of Medicines (CSM) Expert Working Group (EWG) on the Safety of Kava released an extensive report in July 2006 reviewing all available data on kava safety and concluded that the UK's ban on kava products, effective since 2003, should remain unchanged.[1] According to a press release on the UK's Medicines and Healthcare products Regulatory Agency (MHRA) website, "The EWG, the CSM, and the Medicines Commission determined that kava was associated with an unacceptable risk of idiosyncratic hepatotoxicity which could not be minimized or prevented by any regulatory measures other than the removal of kava products from the market."[2]

In the UK, licensed products containing kava (*Piper methysticum* Forst, Piperaceae) as active ingredients were voluntarily withdrawn from sale by manufacturers in 2001, following concerns raised within several countries of a suspected association between kava use and liver hepatotoxicity.[1] According to a UK source, these licenses related to old kava products; no company had licensed kava for reduction of anxiety or stress, the primary use for kava as a phytomedicine as formerly licensed in several EU countries. Because most kava products sold in the UK were unlicensed and sold as foods, safety is a priority and the presence of potentially serious adverse effects is not tolerated; the labeling of these products is not based on an analysis of risk versus benefit, as is done with licensed medicines. Following a review of evidence by the CSM and EWG, the UK government decided to ban all kava products effective January of 2003.[3] The government mandated that evidence regarding kava safety would be reviewed 2 years after this prohibition.[1] The MHRA carried out a public consultation and reviewed available literature regarding kava safety between January and April of 2005. The EWG then met again to consider available data in October of 2005.

At the time of the UK's ban on kava, 68 case reports had been collected from various regulating agencies as evidence of a suspected association between kava use and liver hepatotoxicity. By the time of the EWG's review, this number had risen to 110 case reports. The majority of the evidence consists of spontaneous case reports, which the EWG acknowledges "are anecdotal records and have many limitations." For example, the particular products that were used were not always specified. Unfortunately, the other types of clinical data were not helpful in revealing adverse reactions, and although there has been some evidence of efficacy in clinical trials, these trials have not been helpful in attempts to assess the issue of potential hepatotoxicity. The EWG report concludes that the sum of available evidence strongly suggests a link between kava and hepatotoxicity although no direct causality has been scientifically established. According to the report, "It is the degree of severity associated with some of the case reports that is of greatest concern. Although many patients experienced only mild changes in liver function or jaundice, some patients experienced more serious hepatitis or liver failure that, on 11 occasions, required liver transplants."[1] According to the report, hepatotoxicity directly or indirectly resulted in the deaths of 9 individuals, including 2 of the patients who received liver transplants.

The government mandated that evidence regarding kava safety would be reviewed 2 years after this prohibition.

The EWG considered ways of reducing risk to consumers, but it was not possible to identify at-risk patients and, as unlicensed products, label warnings would have been voluntary, or extracts that would be marketed as medicines would have to be shown to be beneficial in a risk-benefit analysis from a review of both clinical trials and the case reports.

The EWG considered a number of theories regarding the proposed mechanism of hepatotoxicity for kava, but it concluded that all theories lacked direct evidence and require further research. The EWG further argued that, although some studies have attempted to determine a mechanism of hepatotoxicty of kava, such studies have not been conducted in a systematic way and have raised more questions than they have answered. As it is generally well known that there are no recognized animal models for the identification of idiosyncratic hepatotoxicity, the EWG suggested that it might be worth confirming the cytotoxic effects of kava in vivo. The EWG also recommended that future research on the topic "focus on more modern methods which combine metabolic, toxicological, and functional end-points, with particular focus being placed on the chemical moieties responsible for the liver damage, the mechanism by which they cause the damage, and what factors contribute to individual susceptibility."[1]

The MHRA will review any new evidence submitted regarding suspected associations between kava use and liver hepatotoxicity and will reevaluate the kava ban if significant new data are received. The MHRA will also seek expert advice from the recently established Herbal Medicines Advisory Committee (HMAC) as needed. The EWG's 87-page report can be accessed online via the MHRA press release at http://www.mhra.gov.uk/home/idcplg?IdcService=SS_GET_PAGE&useSecondary=true&ssDocName=CON2024228&ssTargetNodeId=663. HG

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FDA Rejects Proposed Health Claim for Cardiovascular Benefits of Green Tea

by Courtney Cavaliere

On May 9, 2006, the US Food and Drug Administration (FDA) rejected a petition for a qualified health claim for green tea (*Camellia sinensis* [L.] Kuntze, Theaceae) that sought permission to allow manufacturers to claim cardiovascular benefits on product labels associated with green tea as a beverage (i.e., as a conventional food) or as a dietary supplement.[1]

The Japanese company Ito En, Ltd. and its US subsidiary Ito En, Inc., which produces and markets green tea, filed the petition a year earlier on June 9, 2005.[2] The petition sought a qualified health claim indicating that daily consumption of at least 5 fluid ounces of green tea as a source of catechins (flavonoids with antioxidant capabilities) may reduce a number of risks associated with cardiovascular disease (CVD). In a letter from Barbara Schneeman, PhD, director of the Office of Nutritional Products, Labeling, and Dietary Supplements of the FDA's Center for Food Safety and Applied Nutrition, the FDA claimed to have reviewed the scientific literature and concluded "that there is no credible evidence to support a relationship between consumption of green tea or green tea extract and a reduced risk of CVD."[1]

The biggest problem with this FDA action is the misinterpretation of the decision by the media and the resulting potential confusion among consumers.

Although Ito En's petition cited 105 publications as evidence to support the health claim for green tea, the FDA argued that many of the documents (i.e., review articles, meta-analyses, book chapters, letters, government reports, and animal and in vitro studies) were not appropriate for drawing scientific conclusions to support a health claim.[1] After discounting what FDA deemed inappropriate, the agency was left with 29 intervention studies on green tea or green tea extract and 10 observational studies. The majority of these were considered insufficient for drawing scientific conclusions, due to poor study design or reporting. According to Dr. Schneeman, the remaining available scientific and clinical evidence was 4 observational studies on green tea (3 of which reported a correlation between green tea and reduced risk of CVD), 3 observational studies on green tea extract (all of which found no evidence of an effect), and 4 intervention studies on green tea (all of which established no evidence of an effect).[1]

Green tea *Camellia sinensis*. Photo ©2006 stevenfoster.com

"The biggest problem with this FDA action is the misinterpretation of the decision by the media and the resulting potential confusion among consumers," said Mark Blumenthal, founder and executive director of the American Botanical Council. "The way it has been reported in the press suggests that FDA has conducted an evaluation on the efficacy of tea and has found it to be ineffective," he said. "This is simply not the case," he added. "What we have here is a regulatory process whereby a company has applied for FDA review and approval of a proposed health claim, and FDA has concluded that not enough clinical data are available to support the proposed health claim to the FDA's satisfaction."

Blumenthal explained that health claims are disease risk reduction statements authorized by the Nutrition Labeling and Education Act of 1990 (NLEA), and as such, are a separate regulatory category distinct from the so-called structure/function claims authorized by the Dietary Supplement Health and Education Act of 1994 (DSHEA). Health claims pertain to both conventional foods and dietary supplements, and are based on the correlation of a nutrient and the reduction of risk of a disease and must be pre-approved by FDA. Structure/function claims pertain mainly to dietary supplements and can be made if the manufacturer believes it has reasonable scientific evidence to support the claim. Structure/function claims do not require FDA pre-approval but the manufacturer must notify FDA within 30 days after introducing the claim into the market.

Although FDA refused to allow a health claim regarding green tea and reduced risk of CVD, its decision has no bearing on green tea's general benefits. The variety of health benefits of green tea were recently reviewed in a 2-part article in the *Journal of Alternative & Complementary Medicine* (which was summarized in a 2-part HerbClip in June of 2006).[3,4] According to one of the article's co-authors, Ray Cooper, PhD, of PhytoScience Inc., such benefits include the following properties, which are supported by some degree of scientific evidence: antiviral and anticancer properties (catechins); anticariogenic (prevention of tooth cavities) effects; potential benefits for weight loss (catechins and caffeine); cardiac health (black tea theaflavins); and arthritis, bone density, and stress reduction (theanine).

According to Dr. Cooper, "Numerous scientific publications now attest to the health benefits of both black and green teas including clinical and epidemiological studies. Firstly, consumption of green tea is generally recognized as safe over a wide therapeutic range (up to 10 cups of green tea per day). Much attention to tea catechins and health has focused on cancer, and drinking tea has been regarded traditionally in Asia, for example, as a generally healthful practice" (e-mail to M. Blumenthal, May 11, 2006).

Notwithstanding the FDA's position on denying cardio health claims, Dr. Cooper states that there is overwhelming evidence from epidemiological and animal studies to attest to the health benefits of green tea in cancer protection.

The overall health benefits of green tea are understandably supported by members of the tea industry. "While the rejection of the Ito En petition has stirred some confusing if not mildly negative media about tea, the fact remains that nutritional experts still consider tea one of the most healthy beverage options on the planet, with its plentiful antioxidants, various minerals and lack of sugar (brewed tea), etc.," said Brian Keating, founder of Sage Group International and publisher of the *Specialty Tea is 'Hot' Report* (e-mail to M. Blumenthal, May 11, 2006). He added, "Consumers and media must understand that tea remains a safe, nutritious and friendly consumer beverage and rejection of one claim filing is not catastrophic." HG

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AHPA Issues Trade Recommendations for Hoodia gordonii, Ginkgo, Pregnancy Labeling, and Internet Sales

by Mark Blumenthal and Courtney Cavaliere

The American Herbal Products Association (AHPA) has issued numerous trade recommendations to its Code of Ethics and Business Conduct in the past several months. AHPA, the leading trade association dealing primarily with herbs and herbal products, has been active in creating self-regulatory initiatives to help standardize practices and ethics in the US herb industry since 1983.[1]

Early this year, AHPA adopted a new trade recommendation regarding raw materials and finished products of *Hoodia gordonii* (Sweet ex Decne, Asclepiadaceae)[2] and modified an established trade recommendation to include extracts of ginkgo (*Ginkgo biloba* L., Ginkgoaceae).[3]

In January 2006, AHPA adopted a policy recommending that the full Latin binomial "*Hoodia gordonii*" serve as the plant's standardized common name (SCN), as opposed to "hoodia," and that this SCN should appear on all labels of *Hoodia gordonii* raw materials, extracts, and finished products.[2] All such product labels should also accurately identify the plant part used, which typically consists of denoting "aerial parts" or "above-ground parts." Such requirements are consistent with US Food and Drug Administration (FDA) regulations. The recommendation also states that ratio terminology on labels of *Hoodia gordonii* extracts must be consistent with established practice and with AHPA's *Guidance for Retail Labeling of Dietary Supplements Containing Soft or Powdered Extracts.*[4] This requires that the first number in the ratio represent the amount of dehydrated starting plant material and the second number represent the amount of finished extract; and further, that such ratios should not be used on any product that is not, in fact, an extract.

"There has been some marketplace confusion about how some *Hoodia gordonii* products are labeled," said AHPA President Michael McGuffin in a press release.[2] "At the same time, none of the elements of this trade recommendation should be surprising or problematic for most companies."

The question may be raised as to why AHPA chose "*Hoodia gordonii*" as the SCN instead of the more convenient "hoodia," which has become the widely used common name in commerce in the United States during the past 3 years. *Hoodia gordonii*, a succulent plant from the arid lands of western South Africa and Namibia, has achieved strong popularity as an ingredient in dietary supplements marketed for weight loss. The federal law governing labeling of dietary supplements states that a plant sold in US commerce, unless already provided with a SCN in AHPA's *Herbs of Commerce, 2nd ed*,[5] must be identified by the Latin binomial. Because *Hoodia gordonii* is not listed in *Herbs of Commerce*, federal regulations require the full binomial be used.[6]

AHPA also amended a trade recommendation regarding known adulterants to include ginkgo extracts in March 2006, listing ginkgo leaf extract with *added* flavonoids (e.g., rutin, quercetin, etc.).[3] In the past few years, there has been mounting concern in the herb trade and among industry analytical chemists that some manufacturers may be adding rutin, a common flavonol glycoside, to ginkgo extracts. These "spiked" extracts may be able to pass chemical specification tests that measure total flavonol glycosides without revealing that the added flavonoids were not contained in the original extract.

According to Steven Dentali, PhD, AHPA's Vice-President of Scientific and Technical Affairs, "There is no problem if anyone wants to market ginkgo extracts with added rutin as long as it is declared in the labeling. However, buyer and seller

should be in agreement as to the identity of articles in commerce and be able to properly verify that identity" (S. Dentali e-mail to M. Blumenthal, May 26, 2006.)

In July 2006, AHPA adopted a trade recommendation that herbal supplements marketed for general retail sale and labeled specifically for use during pregnancy or while nursing contain labeled instructions that encourage pregnant women to discuss use of the product with a healthcare practitioner.[7] This recommendation will go into effect on July 14, 2007. [Note: As part of its Safety Assessment Program, the American Botanical Council has been making such a recommendation since 2002.[8]]

Another trade recommendation relates to Internet sales of dietary supplements.[7] AHPA recommends that any website on which dietary supplements or dietary ingredients are sold identify the company that sponsors the website and provide the company's contact information, including a phone number, mailing address, and e-mail address (if desired). AHPA further recommends that such websites provide the supplement labeling information that is required on dietary supplement products or at least provide a statement that such information is available upon request. All website pages providing statements of nutritional support for dietary supplements available for sale are also recommended to include the standard disclaimer required in the labeling of dietary supplements as mandated by Section 6 of the Dietary Supplement Health and Education Act (DSHEA) of 1994: "This statement has not been evaluated by the FDA. This product is not intended to diagnose, treat, cure or prevent any disease." This AHPA trade recommendation will go into effect on January 14, 2007.

All AHPA trade recommendations are amendments to AHPA's Code of Ethics and Business Conduct. All AHPA members are required to conform to the organization's Code in order to maintain their membership in good standing. The AHPA Code of Ethics is posted online on the AHPA website at http://www.ahpa.org/Portals/0/pdfs/AHPA_CodeOfEthics.pdf. HG

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FDA Denies Medicinal Value of Smoked Marijuana

by Mariann Garner-Wizard

The United States Food and Drug Administration (FDA) issued an unexpected statement on April 19, 2006, saying that the agency does not recognize any legitimate medicinal value for smoked marijuana (*Cannabis sativa, C. indica*).[1] The statement unleashed a strong response from many experts who consider the FDA's release to be evidence of the "politicization" of agency policy in defiance of a growing body of empirical and scientific evidence and opinion.

The FDA's statement included the following:

Marijuana is listed in schedule I of the Controlled Substances Act (CSA), the most restrictive schedule. The Drug Enforcement Administration (DEA), which administers the CSA, continues to support that placement and FDA concurred because marijuana met the three criteria for placement in Schedule I ... (e.g., marijuana has a high potential for abuse, has no currently accepted medical use ... in the United States, and has a lack of accepted safety for use under medical supervision). Furthermore, there is currently sound evidence that smoked marijuana is harmful. A past evaluation by several Department of Health and Human Services (HHS) agencies, including the [FDA], Substance Abuse and Mental Health Services Administration (SAMHSA) and National Institute for Drug Abuse (NIDA), concluded that no sound scientific studies supported medical use of marijuana for treatment in the United States."[1]

Incredibly, the agency adds the statement, "and no animal or human data supported the safety or efficacy of marijuana for general medical use"[1] despite a 1999 review of the literature by the National Academy of Sciences/Institute of Medicine (NAS/IOM) confirming that "Scientific data indicate the potential therapeutic value of cannabinoid drugs for pain relief, control of nausea and vomiting, and appetite stimulation."[2]

The FDA emphasizes that it is "the sole Federal agency that approves drug products as safe and effective for intended indications... Efforts that seek to bypass the FDA drug approval process would not serve the interests of public health."[1]

Medical and Science Experts Criticize FDA's Policy

Response from many sectors of the scientific and medical community was swift and primarily negative. Scientific-American.com's editors promptly started a blog on the topic, with a scathing introductory posting by editor-in-chief John Rennie that recaped recent *Scientific American* articles on cannabinoid research and said the FDA's position is "completely wrong" because "it continues to impede not just the medical use of marijuana but also medical research on marijuana, which could lead to superior therapies that don't involve smoking or getting high at all."[3]

Response from many sectors of the scientific and medical community was swift and primarily negative.

John Benson, MD, co-chairman of the NIH/IOM committee that wrote the 1999 review of marijuana's therapeutic potential and risks, is quoted in Gardiner Harris' article in the *New York Times* as saying that the federal government "loves to ignore our report."[4] The IOM review acknowledged that smoked marijuana is a "crude THC [delta-9-tetrahydrocannabinol] delivery system that also delivers harmful substances" and added, "Until a nonsmoked rapid-onset cannabinoid drug delivery system becomes available, we acknowledge that there is no clear alternative for people suffering from *chronic* conditions that might be relieved by smoking marijuana, such as pain or AIDS wasting."[2]

But in the 7 years since it was issued, most efforts to conduct research on marijuana in the United States have been thwarted by the DEA, which must provide all marijuana used in research, as well as approve the design, objectives, and protocols of all clinical research on the herb.

Donald Abrams, MD, professor of clinical medicine at the University of California at San Francisco, told *The New York Times* that he tried for years to get NIH funding for marijuana research but was repeatedly denied. Eventually, with help from the State of California, Abrams conducted a placebo-controlled trial of marijuana smoking in HIV patients with nerve pain, with good results. However, he has had trouble getting the results of this trial published.[4]

Lyle Craker, PhD, a professor in the Department of Plant and Soil Sciences at the University of Massachusetts at Amherst (and member of the American Botanical Council Advisory Board), applied to the DEA for permission to grow marijuana for researchers because he and other experts have determined that NIDA's marijuana, grown at a high-security government farm at the University of Mississippi at Oxford, is of inadequate quality. Craker's application was denied after a 4-year battle, leading *The Republican* of Massachusetts to comment, "The FDA says there are no sound studies to support the medical use of marijuana, but it is also taking advice from the very agency that is blocking the studies... The DEA has enlisted the FDA in its fight against the legalization of marijuana [for medical purposes], and once again a federal agency that most Americans had trusted to be above politics is in the thick of it."[5]

Sydney Spiesel, MD, a Woodbridge, CT pediatrician and Associate Clinical Professor of Pediatrics at Yale University's School of Medicine, said that, due to the paucity of studies since the IOM report, the FDA's claim to have "definitively established" marijuana's lack of medical value is a case of politics trumping science at the agency, and that it is "certainly not the first time." She cites the FDA's initial decision to block over-the-counter sale of emergency contraceptives, although "overwhelming evidence" found them both safe and effective, and their availability was supported by the FDA's own advisory committee. (The decision was later reversed.) "Marijuana as medicine—whatever its risk and benefits are eventually determined to be—may turn out to be

much less important than the question of whether we can count on agencies like the FDA to be honest...."[6]

Bruce Mirken, communications director for the Marijuana Policy Project (MPP), a Washington-based lobbying group, claimed that the FDA's pronouncement was issued in response to a request by Rep. Mark Souder (R-IN), a critic of medical marijuana legislation passed in 11 states. Souder sponsored legislarion in 2004 which would have required the FDA to produce an opinion on marijuana's medicinal properties. Souder considers medical marijuana legalization a "front for efforts to legalize all uses of it," according to a spokesman in his office.[4]

A bipartisan coalition of 24 Congressional representatives, including Rep. Ron Paul (D-TX) and Rep. Maurice Hinchey (D-NY), wrote a letter to the FDA demanding that the FDA either produce evidence of new research or explain why the statement was issued.[7]

Allen St. Pierre, Executive Director of the National Organization for the Reform of Marijuana Laws (NORML), called the FDA's statement a "lame public relations stunt" and an "attempt to sully 4/20 [April 20], a worldwide celebration day in favor of marijuana, and the opening day of NORML's annual conference." According to St. Pierre, "newspaper columnists and editorial boards around the country are panning the FDA's uber-political denial that medical marijuana is an effective, nontoxic and safe medicine for qualified medical patients" [e-mail, April 26, 2006].

The *Honolulu Star-Bulletin* took the issue more seriously, opining that the FDA's statement may indicate a Bush administration "crack down" on medical marijuana use. "The more than 1,000 Hawaii residents registered to grow and use the plant under their doctors' supervision have reason to feel uneasy."[8]

Making the point that FDA disapproval does not necessarily rest on the best available science, Paul Campos, law professor at the University of Colorado, in his *Rocky Mountain News* column, quotes MPP's Mirken: "The bottom line is that... science at the FDA has given way to politics. They just pretend research evidence for the medical value of marijuana doesn't exist... They're terribly afraid of such research... Continuing to demonize marijuana is the key to the drug war, and the drug war pays the salaries of a lot of people."[9]

Two cannabinoid-based drugs are approved by FDA for use in the United States. Dronabinol, a synthetic version of tetrahydrocannabinol (THC), one of the primary active cannabinoids in marijuana, (made by Roxane Laboratories, Columbus, OH and marketed as Marinol®)

Marijuana *Cannabis sativa* Photo ©2006 stevenfoster.com

and nabilone (another synthetic THC, Cesamet®, Eli Lilly Co.) are approved in the United States to treat chemotherapy-related nausea and vomiting. GW Pharmaceuticals of London, England, maker of Sativex®, a highly-standardized oromucosally-administered cannabis extract, has received FDA approval for clinical trials on Sativex in the United States.[4] Sativex is approved for use as an unlicensed medication in Great Britain and as a licensed drug in Canada (where it is distributed by Bayer). The April 24 e-publication of the *Journal of Pharmaceutical Science* includes a report of the efficacy of cannabis vaporization in delivering beneficial cannabinoids to patients without the toxic by-products of smoking.[10] A new report concludes that smoked marijuana does not increase the risk of developing cancers of the lungs, head, or neck. The study's lead researcher has theorized that THC from marijuana smoke may encourage aging cells to die early, thereby preventing a cancerous transformation.[11] HG

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Functional Food Products and Chronic Diseases

by Danik M. Martirosyan, PhD; Undurti Das, MD, FAMS; and Ashkhen M. Martirosyan

Functional Foods for the Prevention and Treatment of Chronic Diseases, an international scientific conference, was held November 15-16, 2005, in Dallas, Texas. The conference was organized by the Functional Foods Center at Richardson, Texas, along with informational sponsors UNESCO Chair-Life Sciences International Education Center, the Russian Academy of Natural Sciences, and the American Botanical Council (media sponsor). The conference was the second in a series: "Functional Foods: Prevention and Diseases Treatment." Previous scientific conferences have dealt with "Functional Food Products for the Prevention and Treatment of Cardiovascular Diseases," hosted by the Functional Foods Center (held in Dallas, November 2004; see article in *HerbalGram* #66). The result of last year's conference was the publication of 2 books: *Functional Foods for Cardiovascular Diseases* (D&A Inc., April 2005, ISBN: 0-9767535-0-2) and *Functional Foods for the Prevention and Treatment of Cardiovascular Diseases* (D&A Inc., October 2005, ISBN: 0-97675.35-1-0).

The main goal of the 2005 conference was to bring together experts in medicine, biology, and the food industry to discuss the contribution of functional foods in the prevention and treatment of chronic diseases. The scope of the conference covered the advances of phytotherapy and food therapy for cardiovascular diseases, diabetes, obesity, and cancer, with a special focus on the creation of functional and medicinal foods with new properties.

Main conference topics included:

1. The role of nutrition in the occurrence of chronic diseases;
2. How functional and dietary products for the prevention and treatment of chronic diseases are developed and utilized;
3. The creation of functional and medicinal products for the prevention and treatment of chronic diseases (cardiovascular diseases, diabetes, obesity, and cancer);
4. A host of phyto-products and biologically active substances in the treatment of chronic disorders; and
5. A description and various listings of non-traditional plants (i.e., plants that are not well known), which may be used as a source of functional food products.

The conference opened with an introductory speech by the conference chair Dr. Danik M. Martirosyan. It was emphasized that many problems remain unsolved in this area despite the achievements of modern approaches and the potentials of pharmacotherapy. The urgency of chronic diseases, such as cardiovascular disease, cancer, diabetes, and obesity, was stressed along with the necessity for creating functional food based on natural plant-derived resources.

Paul Durfee discussed modern surgical approaches in the war on arteriosclerosis and Kim Rendell discussed "Cardiac Support and Dietary Concerns in the Post Acute Myocardial Infarct Patient" (both are from The Medical Center of Mesquite in Mesquite, Texas). A leading invasive specialist and cardiovascular technician, Mr. Durfee emphasized the achievements of modern surgical approaches and potentials of drug therapy, and pointed out some of the major problems with the current therapeutics (e.g., their unwanted side effects). He also stated that medicine is still unable to treat atherosclerosis effectively despite many advances, and hence, cardiovascular diseases and, in particular, myocardial infarction are the number-one killers in the United States. He noted that there are not enough effective dietary approaches available to offer to post-acute myocardial infarct patients.

Undurti Das, MD, president and CEO of UND Life Sciences (Shaker Heights, OH), spoke on "A Perinatal Strategy to Prevent Adult Diseases: The Role of Long-chain Polyunsaturated Fatty Acids." He proposed that perinatal supplementation of long-chain polyunsaturated fatty acids (PUFAs) prevents or postpones the development of a wide range of adult diseases, including obesity, insulin resistance, hypertension, diabetes mellitus, coronary heart disease, hyperlipidemias, syndrome X, schizophrenia, bipolar disorders, autoimmune disorders such as rheumatoid arthritis and lupus, and inflammatory

bowel diseases, and it protects against the development of certain types of cancers.

Igor Sobenin, MD, with the Institute of Genetic Pathology and Pathophysiology (Moscow, Russia), presented a talk on "Multifunctional Cardioprotective Effects of Time-released Garlic Powder Tablets," made from *Allium sativum* L., Aliliaceae (Allicor®, garlic powder tablets standardized to 1.3% allicin, INAT-Farma, Moscow, Russia). He discussed that an 8-week treatment of 85 patients with arterial hypertension by garlic powder (600 mg daily) resulted in the reduction of both systolic and diastolic blood pressure by 5.2% and 4.0%, respectively. In a hypolipidemic study, the 12-week treatment resulted in a statistically significant decrease in LDL cholesterol by 11.8%, and it was lower by 13.8% as compared to the placebo group. HDL cholesterol increased significantly by 11.5% as compared to the baseline level at randomization. Dr. Sobenin concluded that evidence obtained from these studies indicates that garlic powder tablets have potential in the prevention and control of cardiovascular disorders and are beneficial when taken as a dietary supplement.

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Professor Teruyoshi Yanagita, PhD, from Saga University, Japan, and director of the Japanese Society of Nutrition & Food Science, is a renowned authority on conjugated linoleic acid (CLA) and its health benefits. Professor Yanagita discussed "Conjugated Linoleic Acids and their Health Benefits." His group demonstrated for the first time that the 9c,11t,13c-CLNA isomer reduces apolipoprotein B100 (apoB100) secretion through the suppression of triglyceride synthesis in human liver cells. Apolipoproteins are proteins on the surface of the lipoprotein complex that bind to specific enzymes or transport proteins on the cell membranes. ApoB100 is an intermediate form of lipoprotein and a low density lipoprotein. These results suggest that 9c,11t,13c-CLNA could form an effective dietary regimen for the treatment of hyperlipidemias.

Ravinder Reddy, MD, Associate Professor in the Department of Psychiatry at the University of Pittsburgh, emphasized the role of functional foods in psychiatry. His presentation highlighted key aspects of neuroactive lipid biology and free radical metabolism as relevant to psychiatric disorders, and the role of long-chain PUFAs, particularly omega-3 fatty acids, in the treatment of a variety of psychiatric conditions, particularly schizophrenia and depression.

The conference organizer and first author of this article (D.M. Martirosyan) provided a talk on "Amaranth and Its Oil for the Prevention of Cardiovascular Diseases." The result of these investigations (co-authors: A.V. Pogojeva, K.V. Gonor, S.N. Kulakova, and L.A. Miroshnichenko) showed that oil of the seed of amaranth (*Amaranthus hybridus* L., Amaranthaceae) does not cause allergic reactions or other side effects during its application and lowers cholesterol significantly. Main investigations were conducted in the Russian Institute of Nutrition (Moscow). Eighty patients (60 in the main group; 20 in the control group) suffering from coronary heart disease and hypertension of the 1st and 2nd degrees accompanied by obesity of the 1st and 3rd degrees were under observation. The inclusion of amaranth oil in the diet at the dosage of 6 ml, 12 ml, and 18 ml per day contributed to a statistically significant decrease in the total cholesterol level in the blood serum in patients of main groups by 14%, 17%, and 20%, respectively, and 12% in the control. The application of amaranth oil with the special diet in the patients who had ischemic diseases of the heart, hypertension, and obesity showed a significant hypolipidemic effect. The authors conclude that amaranth oil can be recommended as a functional and dietary food for patients with cardiovascular diseases (arteriosclerosis, ischemic heart disease, hypertension, and hyperlipidemia) and obesity. More studies are needed to investigate the cholesterol-lowering properties of amaranth oil.

The results of the use of dietary supplements and functional foods for the treatment of diabetes were also discussed. Jaime Uribarri, MD, a medical researcher from the Mount Sinai School of Medicine (New York City) discussed "Functional Foods for Diabetes." He proposed to create functional foods for diabetic patients by decreasing the food content of advanced glycation end products (AGEs), well-known pro-inflammatory and pro-oxidant compounds, which may contribute to many of the complications of diabetes. Dr. Uribarri also stressed that because the "main factor responsible for the generation of AGEs in food is the application of heat during cooking, we could modulate the complications of diseases like diabetes in a rapid and cost-effective way by simple modifications of the way we cook."

Motoki Kyo from the Biotechnology Development Department, Toyobo Co., Ltd. (Osaka, Japan) presented a talk about modern methods and equipment involved in investigations in the area of biotechnology and his company's interest in a creation of new functional food products for chronic diseases.

Rakesh Kapoor, PhD, Director of Science and Technology at Bioriginal Food & Science Corp. (Saskatoon, Canada) discussed the role of "Lignans and Alpha-linolenic Acid as Anticancer Food Constituents." These ingredients are present in highest concentrations in flax (linseed) (*Linum usitatissimum* L., Linaceae). Whole flaxseed has limited bioavailability while ground/crushed seeds have a short shelf life, limiting utilization in shelf-stable foods. Bioriginal developed shelf-stable products (Lignamax™ and FibrOmega™) from flaxseed, which are not only rich in these constituents, but are also organic and kosher certified. These products offer advantages to food manufacturers looking for kosher and organic ingredients with health benefits.

One of the most interesting presentations was delivered by investigators from Kaunas University of Medicine (Kaunas, Lithuania). Jurga Bernatonien, PhD, Kristina Ramanauskiene, PhD, and Majiene Daiva, PhD, discussed their interesting results in the report, "The Action of an Antihypertensive Plant Mixture on Metabolic Processes." The aim of this study was to investigate the effect of the infusion produced from lesser periwinkle (*Vinca minor* L., Apocynaceae), the blossoms and fruits of monopistillate hawthorn (*Crataegus monogyna* Jacq., Rosaceae), motherwort (*Leonurus cardiaca* L., Lamiaceae), knotweed (*Polygonum aviculare* L., Polygonaceae), and field horsetail (*Equisetum arvense* L., Equisetaceae) on the carbohydrate-lipid-protein and electrolyte metabolism in aortic myocardial tissues after the induction of pituitrin hypertension in rabbits. It was shown that the infusion prepared from an herbal mixture, which included knotweed, had a curative hypotensive effect. Researchers concluded that administration of an infusion prepared from the herbal mixture containing knotweed normalized arterial blood pressure, decreased hyperlipoproteinemia, hypercholesterinemia, the activity of glycolysis, and decreased cholesterol levels in the aortic wall.

Alexander Orekhov, PhD, Director of the Institute for Atherosclerosis Research in Moscow, Russia, reported on a series of studies that were performed to elucidate the effect of time-released garlic powder tablets in the prevention of acute respiratory disease (ARD). (The report was presented jointly with Dr. Sobenin.) At the first stage, the safety, tolerability, and effectiveness of tablets was investigated in an open-labeled 5-month study in schoolchildren aged 7-16. It has been shown that ARD morbidity (including influenza) was reduced 2.4-fold as compared to the controls. At the second stage, the effects of garlic tablets on ARD morbidity versus placebo or benzimidazole (a pharmaceutical drug) were investigated in the double-blind, placebo-controlled, randomized 5-month comparative study in school children aged 10-12. Research has demonstrated that garlic tablets (Allicor®) reduced ARD morbidity by 2.4-fold as compared to placebo, and by 1.7-fold as compared to benzimidazole. The results of this phase of investigation have demonstrated that garlic powder tablets are effective in non-specific prevention of ARD in children and possess no adverse side effects. Time-released garlic powder tablets (Allicor) are highly recommended for long-term prevention of ARD, especially in health care programs, as an effective, low-cost and safe approach to the improvement of innate immunity and resistance to viral infections.

Conclusion

The general conclusions to be drawn from the various presentations are as follows:

1. More functional food products for the prevention and treatment of chronic diseases such as hypertension, arterioscleroses, cancer, diabetes, and obesity are needed with internationally recognized standards and specifications.
2. More scientific investigations are warranted for the usage of amaranth oil and garlic powder as functional food products for the prevention and treatment of cardiovascular diseases.

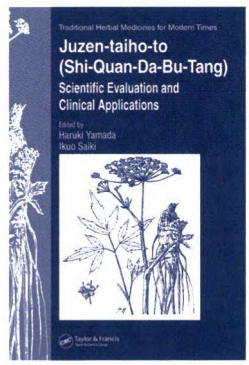
Scientists from countries including Armenia, Czech Republic, Germany, Greece, France, Kenya, Ukraine, and Uzbekistan sent their proposals to the conference organizers and those manuscripts will also be included in the conference presiding and book entitled *Functional Foods for Chronic Diseases*, which will be published in 2006.

The third international conference in the series "Functional Foods for the Prevention and Treatment of Chronic Diseases" is scheduled for October 2006 at the Functional Foods Center in Richardson, Texas. More information about future conferences and new books on this subject are available at www.functionalfoodscenter.net (e-mail: ffc_usa@sbcglobal.net; phone: 469-441-8272). HG

Danik M. Martirosyan, PhD, is a research scientist at the Functional Food Center, Richardson, Texas. Undurti Das, MD, is the president and CEO of UND Life Sciences in Shaker Heights, Ohio. He is also chief editor of the scientific magazine, Lipids in Health and Diseases. *Ashkhen Martirosyan is an editorial assistant with D&A Inc. in Richardson, Texas.*

Juzen-taiho-to: Scientific Evaluation and Clinical Applications by Haruki Yamada and Ikuo Saiki, eds. Boca Raton, FL: CRC Press, Taylor & Francis Group; 2005. 242 pages, hardcover. ISBN 0-415-30830-5. $139.95.

The West has much to learn from the world's many healing traditions. Unfortunately, the challenges found in language, culture, history, and geography have severely restricted Western access to knowledge of Traditional Asian Medicine (TAM), particularly the culturally-specific whole medical systems of Japan, Korea, and Vietnam. Along with China's current version of TCM (Traditional Chinese Medicine), these traditional medicinal systems are based upon published works from ancient China's Han Dynasty (206 BCE-220CE). Despite shared roots, over the past 1400 years these systems have developed independently of one another. This is especially true for Kampo, Japan's traditional herbal medicine system. As a result, it has valuable insights not found in other forms of TAM.



Today, Japan is unique in the world for its widespread use of pharmaceutical-grade, ancient multi-herb formulas, which are sold primarily by prescription. In fact, more than 70% of Japanese physicians routinely prescribe traditional Kampo herbal medicine formulas. More than 145 Kampo formulas are covered by the national health plan. The Kampo tradition is currently taught in 100% of Japanese medical schools and more than 80% of Japanese pharmacy schools. And, today, Japan also leads the world in high-quality pre-clinical research on ancient, multi-herb formulas.

Clearly, Westerners might have much to learn from Japan's Kampo tradition. But how? From whom? And from where? Even in a flattened world, the Japanese language and perspective still represent a nearly insurmountable barrier. Far too few references are available currently in English. Thankfully, the 2 editors and 22 contributors of *Juzen-taiho-to (Shi-quan-da-bu-tang): Scientific Evaluation and Clinical Applications* represent excellent professors who can teach Westerners in English the scientific evidence supporting use of this one important Kampo formula. They bridge the cultural divide using concepts that the Western mind can understand. And for those readers familiar with the Chinese terms for traditional formulas and herbs, the authors include the pertinent Chinese translations throughout the text.

This book opens with an historical and conceptual overview of Kampo medicine and is followed by a chapter describing in thorough detail each of the 10 herbal ingredients in the Juzen-taiho-to formula. Ingredients familiar to readers of *HerbalGram* but with a Japanese twist include the following: cinnamon bark (*Cinnamomum cassia* Blume, Lauraceae); licorice root (*Glycyrrhiza glabra* Linne, Fabaceae, and *G. uralensis* Fisher); Japanese angelica root (*Angelica acutiloba* Kitagawa *or A. acutiloba* Kitagawa var. *sugiyamae* Hikono, Apiaceae); astragalus root (*Astragalus monghol-icus* Bunge or *A. membranaceus* Bunge, Fabaceae); atractylodis rhizome (*Atractylodes lancea* De Candolle and *A. chinensis* Koidzumi, Asteraceae); and Asian ginseng (*Panax ginseng* C.A. Meyer, Araliaceae) root. Other ingredients in Juzen-taiho-to include peony root (*Paeonia lactiflora* Palla, Peoniaceae); rehmannia root (*Rehmannia glutinosa* Liboschitz, Scrophulariaceae); cnidium rhizome (*Cnidium officinale* Makino, Apiaceae); and the mushroom poria (*Poria cocos* Wolf, Polyporaceae). As some of these herbs may not be common in Western herbalism, the descriptions will be of interest to all herbalists. These descriptions include the whole plant, its cultivation, harvesting and processing as well as the macroscopy, the microscopy, general tests, chemistry, pharmacology and traditional uses.

In Japanese *Juzen* means "complete," *taiho* means "big compensation/supplementation," and *to* means "hot water." The name of this traditional herbal medicine could be translated into English as "complete tonifying formula." The therapeutic indications for Juzen-taiho-to appear to be quite consistent. This includes the ancient indications of support for *ki* (chi) and *ketsu* (blood) as well as the modern indications such as for cancer, eczema, and ulcerative colitis. Of broad interest today are the indications for post-operative treatment of malignant tumors as well as treatment for weak constitution, general malaise, and anemia which can accompany therapy for cancet. This discussion of modern uses is followed by several chapters which describe and discuss the *in vitro* and *in vivo* pre-clinical research on this formula. These include the scientific documentation of immunomodulatory, hematopoietic (bone marrow stimulatory), and antibiotic properties.

For many readers, the highlights of this book will be the 3 review chapters which thoroughly address the *in vivo* anti-tumor effects of Juzen-taiho-to on carcinogenesis, tumor progression, and metastasis. This includes thorough discussions of the use of Juzen-taiho-to in combination with chemotherapy and radiotherapy. Surprising to many readers may be the evidence which shows significant reduction in renal and myelotoxicity when Juzen-taiho-to is used with cis-platinum chemotherapy regimens. I appreciated the data comparing efficacy of each of the 10 single herbs from the Juzen-taiho-to formula to the data available on the whole formula. Such infrequently seen scientific data supports the traditional Asian understanding of synergistic or complementary functions of the numerous herbs in multi-herb formulas.

Long before the end of this book, readers will express surprise that so much scientific research supports the use of Juzen-taiho-to in numerous conditions. These readers will want to know why there is not more information about this formula in the United States and other Western countries and why clinical research has not been conducted in the United States. Readers may also want to hear from Japanese physicians who frequently prescribe Juzen-taiho-to. More information on their day-to-day clinical experience, including barriers and clinical limitations to use, would have further strengthened the book for those readers who are unfamiliar with Kampo.

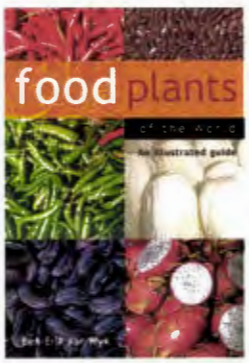
Even without personal reflections from Kampo practitioners, this book represents a much needed entry point into Kampo for interested herbalists and researchers. Fortunately for the West, these authors have translated the original research articles from Japanese into highly-readable English and assembled them into logical chapters for Western readers. The

authors take the reader to the current edge of knowledge on Juzen-taiho-to and the astute reader will recognize the clinical research that remains to be conducted.

The editors and authors have succeeded in creating a book that brings together much of the scientific literature on this one Kampo formula. The extensive endnotes and appendices, well-designed graphs and tables, and skillful editing mean that this book is quite accessible to scientifically-minded audiences. My belief is that this book will motivate readers of *HerbalGram* to learn more about the other 147 national health insurance-covered Kampo formulas (e.g., Sho-saiko-to, Hochu-ekki-to). My hope is that this book will stimulate at least one reader to conduct the necessary clinical research to introduce Juzen-taiho-to into 21st century Western medicine. Should you be that person, let me emphasize that such a shift in consciousness is possible. Currently in the United States, 3 large clinical trials on Sho-saiko-to, Hochu-ekki-to, and Keishi-bukuryo-gan are taking place at major university medical centers. Most remarkably, these are being conducted with United States Food and Drug Administration (FDA) Investigational New Drug status.

Related readings of interest to readers of *HerbalGram* include the previous volume in this series *Sho-Saiko-To: Scientific Evaluation and Clinical Applications* (Taylor & Francis, 2003) and the excellent, newly-published *Introduction to Kampo: Japanese Traditional Medicine* by the Japan Society for Oriental Medicine (Elsevier, 2005). Interested readers should also access the Kampo Medicine Cyber-text/virtual class provided for free by Keio University Medical School at http://web.sc.itc.keio.ac.jp/kampo/vc/index.html. HG

—Gregory A. Plotnikoff, MD, MTS, FACP
University of Minnesota Medical School, Minneapolis
Keio University Medical School, Tokyo



Food Plants of the World: An Illustrated Guide by Ben-Erik van Wyk. Pretoria, South Africa: Briza Publications and Portland, OR: Timber Press; 2005. 480 pages; 1000 color photos. ISBN-13: 978-0-88192-743-6 and ISBN-10: 0-88192-743-0. $39.95.

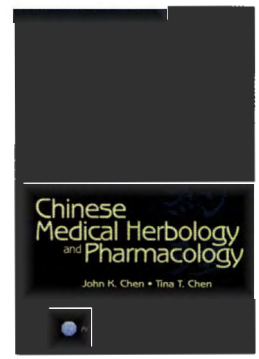
You have to hand it to Briza; for a small South African publishing company, it makes a lot of noise. Briza's success is due largely to mastermind and prolific writer Ben-Erik van Wyk, who does actually write all these books himself—I have seen him doing it—and who has repeatedly proven that he has good sense for what readers want. All of the "Plants" books authored by van Wyk and published by Briza have been successful. Lately, they have been co-produced and co-marketed by Timber Press (USA) and Wissenschaftliche Verlagsgesellschaft (Germany), and for the latter, the books have also been translated into German.

These books may not be textbooks in the traditional sense. They provide quick, accurate, and concise "at a glance" descriptions of the world's (utilized) plant species. The latest—*Food Plants of the World*—consists of one-page monographs on 350 species. Each monograph contains a general description of the plant species, as well as information on its origin, local names, history, cultivation, uses, and nutrient content. Each monograph is profusely illustrated with photographs depicting the plant species, parts used, and/or products derived from it. The monograph section is preceded by an introduction, which provides insights into the origins and classifications of food plants and nutrients. The monographs are followed by a section regarding issues of nutrients, nutrition, and health; a list with short descriptions of plants that didn't make it into the monograph section (i.e., a tabular listing of essential information on food plants which did not merit a monograph); a glossary; a reference list; and an index. All such content provides the reader with fast access to a great deal of well-structured information on a previously underrepresented topic. Here are 3 interesting examples: (1) The flowers of cape pondweed (*Aponogeton distachyos* L.f., Aponogetonaceae) give the characteristic taste to "waterblommetjie bredie," a traditional dish of the South African Cape region; (2) Although its exceptionally nutritious grains are highly valued by Western healthfood fans, grain amaranth (*Amaranthus cruentus* L., Amaranthaceae) is now consumed only in the form of a sweet in its country of origin (Mexico); and (3) The fruit of *Blighia sapida* (König, Sapindaceae), also known as akee in *"akee and saltfish,"* while innocently tasting like scrambled eggs, is highly poisonous unless harvested precisely when ripe and cooked in saltwater before being fried. Readers may be happy to learn that this will definitely not be the last book in van Wyk's "Plants" series. HG

—**Thomas Brendler**
PlantaPhile
Berlin, Germany

Chinese Medical Herbology and Pharmacology by John K. Chen and Tina T. Chen with Laraine Crampton. City of Industry, CA: Art of Medicine Press; 2004. 1267 pages, 1150 illustrations. ISBN: 0-9740635-0-9. $65.50.

This book is an excellent reference text. It is divided into three parts. Part I contains an overview of the history of Chinese herbal medicine; nomenclature; classification; growing, preparation, and processing of herbs; characteristics (taste, etc); clinical applications; and a brief section on concurrent use of herbal medicines and pharmaceuticals. Understanding a bit about nomenclature is useful. Take, for example, the herb *ru xiang* (Gummi Olibanum, frankincense [*Boswellia* spp., Burseraceae]). This book teaches that the name literally means "breast fragrant," both for the form the resin takes as it comes off of the tree and for its fragrance. Chapter 6 (Part I) reviews the characteristics of Chinese herbs. Particularly useful is the table that relates taste to function. For example, the salty taste purges excess, softens hardness, and facilitates entrance to the kidneys, while the bland taste promotes urination. However, the caveat is given that taste does not in fact always indicate function. Chapter 8 (Part I) provides a basic introduction to the concurrent use of herbal medicine and pharmaceuticals. Since many patients presenting for treatment with Chinese herbal medicine will already be taking conventional pharmaceuticals, this topic is clearly relevant.



Part II is laid out in the classical traditional Chinese herbal medicine Materia Medica style, with herb monographs starting with the exterior releasing herbs, and the famous *ma huang* (ephedra) and *gui zhi* (cinnamon). Each chapter contains a thorough preface describing the definition of the category (i.e., exterior releasing herbs), subcategories of action, differential diagnosis and treatment, cautions and contraindications, processing, pharmacological effects, and potential herb-drug interactions. When available, the chemical composition, clinical studies, and toxicology are included as well.

Traditional Chinese herbal medicine, to the surprise of many, includes the use of animal substances and minerals, in addition to the obvious plant material. Animals such as gecko, turtle, and snake appear frequently in commonly used formulas. In the case of gecko, the authors comment about the almost mythical properties ascribed to the tail. They cite studies indicating that both the tail and the body have similar chemical constituents, and are therefore presently used together.

For readers not familiar with the terminology of Chinese herbal medicine, phrases such as liver-calming and wind-extinguishing, or blood-invigorating and stasis-removing seem abstruse at best. This text does not give a deep background understanding of this context, nor should it. Nor does it go into depth regarding the 8 principles used in herbal medicine (hot/cold, interior/exterior, yin/yang, and excess/deficiency). An excellent description of the 8 principles, as well as 8 difficult patterns and syndromes, may be found in Giovanni Maciocia's text, *The Foundations of Chinese Medicine* (Churchill-Livingstone, 1989).

Part III provides 10 valuable appendices. Appendix 1 is a wonderful cross reference of symptoms based on Chinese medicine traditional diagnosis. For example, under abdominal pain one finds a list of herbs broken down by the type of pain, i.e., qi stagnation, blood stagnation, food stagnation, blood deficiency, deficiency and cold, and intestinal abscess. Appendix 2 does the same thing for Western medicine diagnosis. This section is particularly useful, since it is not always easy to understand the diagnosis based on only one or the other system. Appendix 3 goes a step further, cross referencing based on pharmacological effects (the first author is a pharmacist, doctor of oriental medicine, and an acupuncturist). Appendixes 4 and 5 are a cross reference of the *pinyin* single herb names and the names of traditional formulas discussed in the book, respectively. Appendixes 6 and 7 discuss the use of herbs that either support pregnancy or are contraindicated during pregnancy.

Appendix 8 provides dosing guidelines, based both on age and weight. Appendix 9 sorts out weights and measures. (Who knew that 20 grains equals 1 scruple, unless one were a pharmacy historian?)

Included at the end of the book are bibliographies of historical and contemporary references. There is also a useful glossary. (The glossary does not contain some of my favorite Chinese medicine phrases such as "running piglet syndrome." Another of my favorites, Plum pit syndrome (or qi) is

translated as "globus hystericus," a term now often replaced with the less pejorative "globus sensation.")

The book provides additional resources such as color photographs of each herb in the beginning of the book, and black and white photographs of each herb accompanying the individual monographs. These are particularly useful as a memory jogging tool. One can easily become bogged down with pin yin, Latin, and common names of plants. Having a picture to relate to adds an additional memory hook. When one is able to visualize the image of the plant, it is often easier to recall other details, such as botanical and common name, and the myriad of uses ascribed to the plant.

This is not a how-to-book for the beginning physician who wants to know more about Chinese herbs. It comprises the first year of material that is covered in the 2-year, 450 hour National Certification Commission for Acupuncture and Oriental Medicine course in traditional Chinese herbal medicine. As a reference, it also includes helpful appendices such as a cross reference based on traditional Chinese medicine diagnosis, western medical diagnosis, and pharmacological effects.

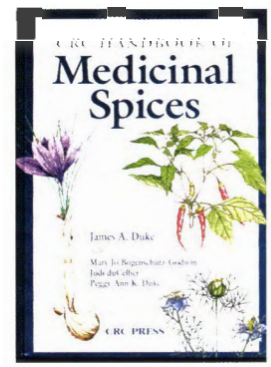
For the herbalist or physician wishing to dive deep into the complex and enormous world of traditional Chinese herbal medicine, this is a necessary book. However, while the casual user may find the information useful in an encyclopedic way, he or she may also experience the book as relatively inaccessible without the formal training that accompanies classroom herbal education. If the practitioner is beginning to use some simple traditional Chinese medicine formulas in his/her practice, such as Gan Mao Ling, or Yin Chiao, then this book will serve as a useful reference to understanding the properties of each of the individual constituents of the formula. It may also serve as a source text for medical doctors with the need to understand the Chinese herbal formula that their patients may be taking.

The company can be reached at their Web site at www.aompress.com. Samples of various sections of the text are posted on the site in PDF format. HG

—Robert A. Schulman, MD,
Clinical Assistant Professor of Rehabilitation Medicine and Complementary/Integrative Medicine, Weill Medical College of Cornell University, New York

CRC Handbook of Medicinal Spices by James A. Duke with Mary Jo Bogenshutz-Godwin, Judi duCellier, and Peggy-Ann K. Duke. Boca Raton, FL: CRC Press; 2003. 360 pp., hardcover. ISBN 0-8893-1279-5. $139.95. ABC Item#B532

Jim Duke has a remarkable ability to take volumes, reams, and gigabytes of information, distill the method and madness down to keywords, and transform the essence of the information into short abstracts peppered with observations or opinions that bring flavor to what otherwise might be boring scientific diatribes. This guide by Emeritus ABC Board of Trustees member and ethnobotanist elite Jim Duke and colleagues covers 60 popular spices, organized by scientific name. It includes sections on common name, medicinal activities and indications, multiple activities, other uses (particularly culinary uses), cultivation, phytochemistry and constituents, and compound activity. Duke cooks phytochemistry down to its practical potential and pulls pertinent ethnobotanical facts to the surface like a gardener pulls weeds.



After a lifetime of Duke's cajoling and massaging of the vast scientific literature on medicinal plants and what makes them tick, we are the beneficiaries of the morsels of information that have risen to the surface. Duke and his colleagues create a rich stew of information on each of the 60 spices treated in this book. In a single sentence, one can find humor, home remedies, and research leads. For example, the author points out that greater galangal (*Alpinia galanga* [L.] Sw., Zingiberaceae) is "useful in pediatric respiratory problems. I would not hesitate to mix it with those [anise and dill] for my grandchildren during flu season [if only your children would let you, Jim] . . . . . As a paste, with a little garlic and vinegar (red wine vinegar is better), it is a last resort drastic remedy for herpes." And on it goes.

You have to learn how to read Duke's various CRC Handbooks, including this one. His comments, beliefs, and opinions can be found at any point in the text. He doesn't need to be convinced by a double-blind, randomized, placebo-controlled study that garlic (which he calls "Russian penicillin") is a drug of choice to "prevent or reduce the likelihood of getting anthrax if you have been hit with 8000 spores." What is not opinion is referenced, either using the author-date system or with 3-letter abbreviations for books and journals, which he cites on a regular basis. It looks cumbersome on the printed page, but if you keep a finger stuck in the abbreviations keys and refer to them while reading, the embedded codes soon make good sense. If a phytochemical is listed for a plant, information on its bioactivity or toxicity with citation is also included. Duke suggests that myrtle (*Myrtus communis* L., Myrtaceae) may be useful for infections. He then enumerates 15 biologic activities that lead him to his conclusion, each followed by a list of phytochemicals in the plant to which that pharmacologic activity has been attributed. I had for the most part dismissed my myrtle plant as nothing more than an evergreen ornamental taking up room in a plant pot, but in these pages I find it is a veritable pharmacopeia used for more medicinal, culinary, and ornamental uses than any collection of books has ever before revealed to me. Here we find food and flavoring uses from Sardinia, Jerusalem, Damascus, Italy, Corsica, and Crete. We find uses by Jews, Arabs, Turks, Russians, and Greeks. "The leaves are used for massage to work up a glowing skin." Where else are you going to find this kind of information except in a book by Duke? As for cultivating the plant, you will learn its best horticultural uses, soil type, pH, propagation methods, how to get it through the winter in the North, and when it should be pruned. The horticultural information is detailed and valuable.

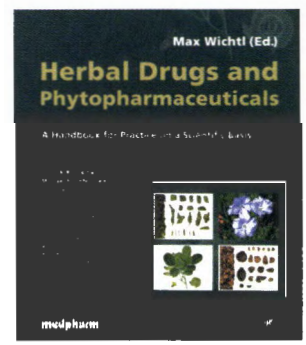
Throughout the book one finds cross-referencing to other Duke CRC handbooks and his always-expanding USDA database (one of the most widely used databases of that behemoth government agency, available at http://www.ars-grin.gov/duke/). "I'm not going to pay nearly $140 for a 348 page book!" you might say. How much did you spend on dinner last night for you and your dinner companion? For me the choice is easy. If a book has Jim Duke's name on it, I buy it—simple as

that. The hard choice is whether to keep it on the shelf with medicinal plant reference books, or have it at home next to the spice shelf as an inspiration for new ideas and new uses for favorite spices. You will discover more within these pages than Columbus ever did by sailing west. HG

—**Steven Foster,**
President of Steven Foster Group, Inc., Eureka Springs, AR

Herbal Drugs and Phytopharmaceuticals. 3rd English ed., by Max Wichtl (ed). Josef A. Brinckmann and Michael P. Lindenmaier, translators. Stuttgart, Germany: Medpharm Scientific Publishers; Boca Raton, FL: CRC Press, 2004. 704 pp., hardcover. ISBN 0-8493-1961-7. $279.95. ABC Item#B527

"Wichtl and Bisset," as the previous English editions of *Herbal Drugs and Phytopharmaceuticals* (translations of rhe German editions of *Teedrogen und Phytopharmaka*) have come to be known, are considered standard English-language references on the identities, origins, constituents, preparations, uses, and regulatory statuses of ingredients used in herbal teas and phytomedicines. Several years passed between the last English edition and publication of the third and fourth German editions. The present translation is of the fourth German edition and includes 212 monographs of herbal drugs and phytomedicines. As author Max Wichtl states in the preface to the third English edition, "two recognized specialists, Josef Brinckmann and Michael Lindenmaier, accepted the task to translate the new German edition in English. The translators did not only translate the text very precisely but also adapted the entire book to include pertinent British, Canadian, and US regulations for herbal products."



Herbal Drugs and Phytopharmaceuticals is a book that has already stood the test of time since the appearance of the first English edition, 12 years ago, translated by the late Prof. Norman Grainger Bisset of the University of London. The book had a particularly strong European focus and provided details on the identities and uses of many European phytomedicines then emerging into the American market. The present, third English-language edition, as Dr. Wichtl has pointed out, not only provides a precise translation of the German edition, but also adds specific perspectives from the ingredients' trade and regulation in English-speaking countries. What's more, the language skills and industry experience of the translators provide a sharpening of detail nuance that heightens its value to those who handle the wide range of ingredients covered here on a daily basis. In this edition there is considerably more information, reflecting the rapid advancement in the scientific literature on medicinal plants in the past decade. The result is a tome that is more than 150 pages longer than the first English edition. The constituents and indication sections have been extensively revised and 32 new monographs have been added, compared to the second English edition. The text has also benefited from the contributions of many academic,

New Book Profiles

British Herbal Compendium: A Handbook of Scientific Information on Widely Used Plants. Vol 2. Peter Bradley. Bournemouth, England: British Herbal Medicine Association; 2006. 409 pages, softcover, contents, chemical structures, references, index. £59.50 (approx. $112.00). ISBN 0-903032-12-0.

This long-awaited second volume contains 80 therapeutic monographs on widely used medicinal plants. Each monograph includes chemical constituents (with structure diagrams), pharmacology and clinical studies, therapeutics, safety data and regulatory status. More than 3000 full citations are included.

Pomegranates: Ancient Roots to Modern Medicine. Navindra P. Seeram, Risa N. Schulman, and David Heber, eds. Boca Raton, FL: CRC Press, Taylor & Francis Group; 2006. 244 pages, hardcover, contents, b&w figures, tables, chemical structures, references, index. $129.95. ISBN 0-8493-9812-6.

Explores the biochemistry and health effects of pomegranates. Identifies more than 100 phytochemicals in the fruit. Includes information on laboratory, animal, and human studies of its antioxidant effects on cardiovascular disease. Addresses research on pomegranate's ability to fight several types of cancer. Substantial sections on commercialization, plant growth, and improvement. Discusses research on the bioavailability and metabolism of pomegranate polyphenols in humans.

Handbook of Cannabis Therapeutics: From Bench to Bedside. Ethan B. Russo, MD, and Franjo Grotenhermen, MD, eds. New York: Haworth Press; 2006. 471 pages, softcover, contents, b&w figures, tables, references, index. $39.95. ISBN 0-7890-3097-7.

Provides a brief history on the medicinal uses of cannabis (marijuana). Includes a compilation of articles from the *Journal of Cannabis Therapeutics*, formerly edited by the author. Presents pharmacology, pharmacokinetics, biochemistry, toxicology, side effects, and potential clinical uses of cannabinoids. Each chapter contains references and updated bibliographies.

Ampalaya: Nature's Remedy for Type 1 and Type 2 Diabetes. Frank Murray. Laguna Beach, CA: Basic Health Publications, Inc.; 2006. 217 pages, softcover, contents, glossary, appendix, resources, references, index. $14.95. ISBN 1-59120-178-0.

Focuses on preventing or controlling type-2 diabetes with lifestyle changes and the use of ampalaya (*Momordica charantia*), a vegetable with blood sugar-lowering properties. Animal and human studies are presented on the effects of ampalaya, commonly known as bitter melon, bitter gourd, or vegetable insulin,

industry, and professional experts in Europe. Seven herbs are appended in a section called "Short Monographs," which are deemed by Wichtl to be "of relatively minor importance for Central Europe," yet include such important items as saw palmetto (*Serenoa repens* [W. Bartram] Small, Arecaceae) berries, black cohosh (*Actaea racemosa*, syn. *Cimicifuga racemosa* L., Ranunculaceae) rhizome, feverfew (*Tanacetum parthenium* [L.] Sch. Bip., Asteraceae) herb, and gotu kola (*Centella asiatica* [L.] Urb., Apiaceae). Such monographs seem to be of a little more than just passing importance! It seems odd that they are placed in a section best described as an afterthought, rather than developed as full monographs. Cola nut (*Cola* spp. Schott & Endl., Sterculiaceae) is also included here, and although perhaps not an important phytomedicine, it is certainly an important natural ingredient in numerous formulations, especially in dietary supplements in the United States. European sanicle (*Sanicula europaea* L., Apiaceae) and purple loosestrife (*Lythrum salicaria* L., Lythraceae), also included in this section, are certainly not on anyone's "A" list. One would hope that future editions produced for German consumption might contain information on ginseng and include American ginseng (*Panax quinquefolius* L., Araliaceae) and Asian ginseng (*P. ginseng* C.A. Mey., Araliaceae) as separate monographs, as has now been done with the monograph on tea (*Camellia sinensis* [L.] Kuntze, Theaceae), which includes distinct entries for black tea and green tea. And some of the English-reading users will be surprised (and disappointed) once again to find that botanicals that never reached "herbal drug or phytomedicine" status in Germany, such as goldenseal (*Hydrastis canadensis* L., Ranunculaceae), are completely absent. And after 4 German editions and 3 English editions, still no separate chapter on *Echinacea purpurea* ([L.] Moench, Asteraceae)?

Returning to what's in the book, instead of what you won't find: each monograph contains details on plant sources, synonyms, origins, constituents, indications, making the tea, tea preparations, phytomedicines, authentication, adulteration, storage (if relevant), along with literature references (titles of articles excluded). Regulatory status and TLC (thin layer chromatography) identification are often included. The book is richly illustrated with 519 color images (of varying quality), over 300 black and white illustrations, and 447 chemical structures. When communicating with various individuals over the years regarding their libraries, one often discovers that yes, a particular title is in that person's institutional, company, organizational, or personal library. However, it is always surprising to learn that the title one possesses is 1, 2, or 3 editions out of date! With such a rapidly changing information landscape in the medicinal plant field, it is particularly important to obtain new, revised editions of previous works. Often they are completely different works from earlier editions of the same title. Such is the case with the third English edition of Wichtl. If you don't have this edition, you simply don't have Wichtl. Break into your savings, raid the corporate coffers, or see your loan officer for the $279.95 price tag that might break the piggy bank. But if you deal with herbal drugs and phytopharmaceuticals of European (particularly German) market origin, this book is a must-have resource. HG

—Steven Foster,
President of Steven Foster Group, Inc.,
Eureka Springs, AR

as well as a selection of stories profiling diabetics who have incorporated ampalaya successfully into their diet.

Eating and Healing: Traditional Food as Medicine. Andrea Pieroni and Lisa Leimar Price, eds. Binghamton, NY: Food Products Press; 2006. 406 pages, softcover, contents, b&w photos, figures & tables, references, index. $39.95. ISBN 1-56022-983-7.

Presents biological and cultural aspects of food as medicine from around the world, such as in Tibet, Cuba, Italy, and Africa. Each chapter is written by a different contributor and presents scientific research about medicinal foods from a specific area of the world, along with traditional information gathered from locals. Some chapters also discuss issues of globalization and the loss of healing food knowledge.

Emphysema and Chronic Obstructive Pulmonary Disease: Therapeutic Approaches through Nutrition, Natural Medicine, Alternative Medicine. Robert J. Green Jr., ND. San Diego, CA: Aventine Press; 2005. 212 pages, softcover, contents, tables, b&w figures, appendices, bibliography, glossary, index. $19.95. ISBN 1-59330-332-7.

Primarily written for patients diagnosed with chronic obstructive pulmonary disease (COPD) or emphysema, this book is also a helpful tool for healthcare professionals. Focusing exclusively on natural health and nutrition, the author presents scientifically- and historically-based treatments. Diet and nutrition therapy, nutrition supplementation, herbal medicine, exercise and physical therapy, as well as other alternatives are also discussed.

Medicinal Plants of the Southern Appalachians. Patricia Kyritsi Howell. Mountain City, GA: Botanologos Books; 2006. 262 pages, softcover, contents, glossary, bibliography, resources, bloom & harvest calendars, therapeutic index, index. $19.95. ISBN 0-9774905-0-5.

Includes the historical and current uses of 45 medicinal plants. Profiles of each plant also include harvest information, preparations and dosages, and detailed medicine-making instructions for many of the plants.

Sacred Plant Medicine: The Wisdom in Native American Herbalism. Stephen Harrod Buhner. Rochester, VT: Bear & Company; 2006. 208 pages, softcover, contents, b&w photos, references, suggested readings, index. $16.00. ISBN 159143058-5.

Filled with photos and extensive quotes, Buhner explores the interactions of Native Americans and plants, including profiles of many of the plants considered sacred by the tribes. Their traditional uses are addressed, including preparations and dosages, along with ceremonial elements such as prayers and songs associated with each plant. HG

Lynn Zimmer 1947–2006

Lynn Zimmer, PhD, a respected sociology professor, author, and spokesperson for the drug reform movement, died on July 2, 2006, at the age of 59.[1]

Lynn Etta Zimmer was born on May 20, 1947, in Rochester, NY. She earned her bachelor's degree from the State University of New York at Cortland in 1977, followed by her master's and doctoral degrees in sociology from Cornell University in 1980 and 1982, respectively. Her doctoral thesis examined the integration of women guards into the US prison system and resulted in her first book, *Women Guarding Men*, in 1986.

Dr. Zimmer taught at the State University of New York at Geneseo from 1982 to 1990, and then served on the faculty of Queens College of the City University of New York from 1990 to 2002. Early in her professional career, she began to examine the drug testing industry and US drug policies.

"Lynn did an excellent study of Operation Pressure Point, the NYPD's drug sweep initiative on the Lower East Side during the mid-1980s," said James Jacobs, PhD, law professor at New York University and Dr. Zimmer's doctoral adviser at Cornell (e-mail, August 17, 2006). "I think it was that study that launched her into the work on drugs and drug policy. In that area, she made many major contributions."

Dr. Zimmer became actively involved in the Princeton Group for the Study of Drug Policy, the Drug Policy Foundation (now the Drug Policy Alliance), and the National Organization for the Reform of Marijuana Laws (NORML). She wrote multiple monographs, articles, and book chapters on issues of drug testing, drug policies, and drug reform. She also coauthored the book *Marijuana Myths, Marijuana Facts: A Review of the Scientific Evidence*, in 1997 with John P. Morgan, MD, professor of pharmacology at the City College of New York.

Dr. Jacobs explained that this book became widely successful and has been translated into several foreign languages. "It has been fantastically influential. *Marijuana Myths* catapulted Lynn into real prominence. She appeared on many TV shows, including some very prominent ones, and on radio and in public appearances. She did a couple of European tours talking about the book and drug policy issues," he said.

According to Dr. Morgan, Dr. Zimmer's greatest contribution was her analysis of the "drug abuse establishment" (DAE). "She early on realized that many individuals and organizations owed their political lives, their reputations, their prestige, their status, their income, and their jobs to fighting the war on drugs," Dr. Morgan explained (e-mail, August 16, 2006). "She described this massive entity (the DAE) in bureaucratic terms and realized that its chief function was to preserve and empower itself. Shortly before her death, she gave a copy of a manuscript regarding the DAE to a student, who had become one of her best friends and who is working hard to prepare it for publication."

Dirk Nelson, a former licensed clinical social worker and long-time activist in the drug reform movement, attended the Drug Policy Foundation's 13th International Conference on Drug Policy Reform in 2000, where Dr. Zimmer received the Lindesmith Award for Achievement in the Field of Scholarship. Nelson was left with strong impressions of her character and eloquence. "People who can speak unapologetically with her grace, insight, and humor on this topic, with her kind of credentials, are often difficult to find," he said (oral communication, August 18, 2006). "Her contributions to the movement, to end the unreasonable punishing of people for their pharmacological adventures, were invaluable." Dr. Zimmer also received the Lester Grinspoon Award for Achievement in the Field of Marijuana Law Reform from NORML in 2000.[1]

Dr. Zimmer was diagnosed with multiple sclerosis (MS) in the late 1990s. "MS took a terrible toll on her," said Dr. Morgan. "It robbed her of her ability to see and to move about in the world. It did not affect her ability to think and teach and be kind. She was the best person I have ever known."

Dr. Zimmer is survived by her two sons Joseph and Mark. HG

— **Courtney Cavaliere**

Reference

1. Nadelmann EA. Lynn Zimmer 1947-2006. Drug Policy News. Drug Policy Alliance Web site. Available at: http://www.drugpolicy.org/news/070506lynnzimmer.cfm. Accessed August 11, 2006.

Robert Daniel Winn 1927–2006

Robert Daniel (Dan) Winn, a strong supporter of herbal medicine research and medicinal plant refor-

estation, died on March 21, 2006, at the age of 78. He suffered a fatal head injury as a result of a fall he sustained in Nairobi, Kenya, while he and his wife Diane were attending a conference on herbal antimalarials. The conference participants dedicated the proceedings to Dan.

Diane had been invited to speak at the conference about the work she has been doing in Ghana with *Cryptolepis* (Asclepiadaceae), which is a potentially effective herbal antimalarial medicine that could eventually benefit millions of children across Africa (See article in *HerbalGram* 60).[1] Dan had been intensely supportive of her work and accompanied her to Ghana on most of her trips.

Dan and Diane shared a passion for research into traditional plant medicines of Ghana. Being a patent attorney, he was always looking for intellectual property in any of the developmental work done on the vast body of traditional knowledge on West African herbal medicines that Diane received from the late Ghanaian traditional herbal medicine expert Oku Ampofo, MD, with whom Diane had worked when she was in Ghana in the Peace Corps in the 1960s.

Diane will continue to pursue this work, and if successful, it will be a legacy to Dan's vision and commitment. Diane has established a "Dan Winn Memorial Foundation," and the first effort on behalf of the foundation will be to establish a "Dan Winn Memorial Agroforestry Centre" in Ghana, so that his passion for plant medicines and reforestation can live on. This will be the first agroforestry center to reforest with medicinal plants and trees—a potential future site for ecotourism in the area.

Dan grew up in Dallas, TX, and served in the Army before graduating from Rice University and the University of Texas Law School. He became a patent attorney in Houston in 1952. He moved to McAllen, TX in 1959 with his wife and three children, where he became president of a mortgage company. His most notable achievements include building the first enclosed shopping mall in the Rio Grande Valley and creating Medico, a regional chain of drugstores.

Dan loved hiking in England, driving his Morgan, and dancing the Sweet Swing to Glenn Miller's Orchestra. He loved beautiful cars, airplanes, and all things mechanical.

Dan is survived by his wife Diane, his son Robert Daniel Winn, Jr., his daughter Susan Winn Lowry, two grandchildren, his brother William Edward "Ted" Winn, Jr., and his sister Marjorie Winn Ford.

Memorials may be given to PlantSearch International Foundation—Dan Winn Memorial Fund for Herbal Antimalarial Research in Africa (check should be made to "PSIF" with "Dan Winn Memorial Fund" in the memo field), sent in care of Irvin Coker, 9501 Brunett Avenue, Silver Spring, Maryland 20901. HG

Reference

1. Addy M. Cryptolepis: an African traditional medicine that provides hope for malaria victims. *HerbalGram*. 2003;60:54-59,67.

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October 3-7: Contributions of African Botanica to Humanity 2006. N'Zérékoré, Republic of Guinea, West Africa. This event will study in detail the pharmacological, phytochemical, and genetic aspects of African botanica to clarify the intimate structure of plants' molecules and to identify interesting characteristics of plants used for health maintenance. This symposium will also give plant reproduction specialists the opportunity to share their views about the agronomical aspects that can influence the content in bio-active compounds in medicinal, aromatic, and food plants. Web site: http://www.botaniqueafricaine.com/. Phone: 506-455-4110.

October 5-8: 5th Annual Traditional Chinese Medicine Conference. East Rutherford, NJ. "Building Bridges of Integration for Traditional Chinese Medicine—Transformation: Spirit in Healing" is a landmark educational forum on traditional Chinese medicine for Eastern and Western healthcare professionals interested in exploring this medical system's growing role in integrative and complementary healthcare. It will take place at the Sheraton Meadowlands Hotel, East Rutherford, NJ, just outside NYC. Web site: www.tcmconference.org. Phone: 1-888-TCM-6909.

October 6-8: Neuroprotection, CME Course. Scottsdale, AZ. Functional medicine can help with prevention, risk reduction, stabilization, and sometimes regression of patients' neurological conditions. This course is intended to help healthcare providers extend the practice of functional medicine to patients diagnosed with neurological conditions. Presented by the Institute for Functional Medicine. Web site: www.functionalmedicine.org. Phone: 800-228-0622.

October 8: The 5th Annual Catskill Mountain Ginseng/Medicinal Herb Festival. Catskill, NY. The keynote speaker will be Scott Persons, author of *American Ginseng Green Gold*. Joining him will be David Taylor and Andy Hankin. For directions or lodging information contact Linda Overbaugh at the Heart of Catskill Association. E-mail: HOCA@mhonline.net. Phone: 518-943-0989.

October 9-15: CancerGuides. Bloomingdale, IL. CancerGuides is the world's first and only comprehensive training program in integrative oncology. This unique interdisciplinary course teaches health professionals and patient advocates to work collaboratively with people with cancer to create safe, effective, humane, individualized programs of care that integrate the best of complementary and alternative approaches with conventional therapy. Web site: www.cmbm.org.

October 13-15: Holistic World Expo. Toronto, Canada. The Holistic World Expo is intended for both the public and healthcare professionals. It will feature presentations from international leaders and speakers, as well as numerous exhibitions and hands-on demonstrations that provide a well-rounded view of holistic health benefits. This event will provide information for people interested in enhancing their health, de-stressing their lives, and focusing on their spiritual well-being. For more details visit www.holisticworld.org.

October 14: One-Day Workshop Planetary Herbalism. London, UK. Dr. Michael Tierra LAc., OMD, the renowned herbalist and creator of the Planetary Formulas range, will conduct this workshop. Dr. Tierra will specifically focus on the topic of integrating herbs and traditional assessment methods for maintaining health and treating disease. This event will be held from 9:30-4:30 at Herringham Hall, Regent's College. Dr. Tierra will also be a key speaker at CAM EXPO 2006 at Excel, London Docklands, Oct 15-16. Phone/Fax: (0) 1873 851953. E-mail: info@earthforce.com. Web site: www.earthforce.com.

October 14-15: 3rd International Conference: Functional Foods and Phytotherapy for Chronic Diseases. Dallas, TX. The main goal of the conference is to bring together experts in medicine biology and the food industry to discuss the prevention and treatment of chronic diseases. The conference will cover the advances of phytotherapy and food therapy for cardiovascular disorders, diabetes, obesity, and cancer, with a special focus on the creation of functional and medicinal foods with new properties. Web site: www.functionalfoodscenter.net.

October 16-19: International Symposium on Pomegranate and Minor Mediterranean Fruits. Adana, Turkey. This event, which will be held on the campus of Cukurova University, will feature lectures and workshops on issues relating to pomegranates and Minor Mediterranean plants. Topics include plant physiology, current research, harvesting, economics, and pests and diseases, among others. For more information, contact Dr. Ahsen Isik Özgüven; Phone: (90)3223386564. Fax: (90)3223386388. E-mail: ahsen@cu.edu.tr. Web site: www.cu.edu.tr/fakulteler/zf/bkb/ispm/.

October 18-20: SupplySide West 2006. Las Vegas, NV. SupplySide West is a 3-day event offering industry the opportunity to learn about the latest innovative and healthy ingredients, meet new vendors and formulators in the 850+ booth exhibit hall, and source ingredients, packaging, labeling and private-label manufacturing services in one location. For more information, please contact Amy Sharman with Virgo Publishing at (480) 990-1101 ext. 1543. Web site: http://www.supplysideshow.com/west/.

October 24-25: Food Law & Regulation. Chicago, IL. This new conference organized by the publishers of *Food Chemical News* will introduce food industry executives to the latest updates on hot legislative issues impacting the food industry and enable participants to debate and analyze major food safety and regulatory issues. Attendees will have the opportunity to hear the latest news and views from key industry stakeholders, legal experts, consumer groups, and government agencies. Phone: +44 (0) 20 7017 7500, E-mail: sophie.stevens@informa.com. Web site: www.agranet.com/FLR06.

October 26-27: Malta Polyphenols 2006. Malta. This international conference, which combines 3 different events on polyphenols organized in parallel, will present the latest advances on polyphenols and their effects on health. For more information or to view the conference program, visit the Web site: www.isanh.com. E-mail Dr. Sandrine Rodriguez: sfa-paris@wanadoo.fr.

October 26-27: Regulations for Nutraceuticals Conference. Chicago, IL. Nutraceuticals, functional foods, and dietary supplements have become a rapidly growing segment of the food market over the past several years. Learn how to maximize the success of a new product launch and navigate the FDA's regulatory process. For more information visit the Web site: www.intertechusa.com.

October 27-29: American Herbalists Guild's 17th Annual Symposium. Boulder, CO. AHG's annual symposium is widely regarded as one of the preeminent conferences on botanical medicine, offering over 40 workshops by leading practitioners and researchers. AHG also expects to offer continuing education credits for nurses, pharmacists, acupuncturists, nutritionists, and naturopathic physicians. More information about the symposium is available at www.americanherbalistsguild.com.

October 28: Natural Source International's Symposium. Columbia University, NY. This 10th anniversary symposium will give participants the opportunity to learn more about the past, present, and future of the research begun by Mirko Beljanski, PhD, of the celebrated Pasteur Institute in Paris, France. Featured lecturers will include Columbia University's director of the Center for Holistic Urology, Aaron Katz, MD, author of *Dr. Katz's Guide to Prostate Health*, and Michael Schachter, MD, head of the Schachter Center for Complementary Medicine. To register, visit the Web site: www.natural-source.com. E-mail: info@natural-source.com. Phone: 212-308-7066.

October 28-30: The 2nd International Symposium on Saffron Biology and Technology (ISSBT). Mashhad, Iran. This symposium is intended for those involved in the production, processing, marketing, or medicinal use of saffron. Organizers for the event are the Center of Excellence for Special Crops (CESC) Faculty of Agriculrure and Ferdowsi University of Mashhad (FUM) under the auspices of the International Society for Horticultural Science (ISHS) Section of Medicinal and Aromatic Plants. Web site: http://saffron-ir.um.ac.ir/.

October 28—November 3: The Science and Clinical Application of Integrative Holistic Medicine Conference. San Diego, CA. This accredited program encourages academics and healthcare professionals from around the country to learn evidence-based and in-depth knowledge of the growing field of integrative holistic medicine. Presented by Scripps Center for Integrative Medicine and the American Board of Holistic Medicine. Contact: Julie Simper, Phone: 858-587-4403. E-mail: simper.julie@scrippshealth.org.

October 29—November 1: The 4th International Conference on Mechanism of Action of Nutraceuticals (ICMAN4). Tel-Aviv, Israel. The conference will deal with the latest developments in dietary and endogenous sources of nutraceuticals; the results of cellular, molecular, and animal studies in diabetes, cancer, neurodegenerative disease, cardiovascular and inflammatory disorders; proteomic-genomic developments; and anti-aging opportunities. Web site: http://www.evetopf.org/icman4.

November 5-8: Worldnutra Conference and Exhibition. Reno, NV. The scientific

program will be comprised of plenary sessions from keynote speakers and oral presentations from industry, academic, and government representatives. It will cover the latest developments in nutraceuticals, functional foods and ingredients, processing, health aspects of antioxidants, and herbal extracts. The industry exhibition will display the latest technology, ingredients, food products, equipment, and services available in nutraceuticals and functional foods. Web site: www.worldnutra.com.

November 10-11: Realizing Nature's Potential: The Once and Future King of Drug Discovery Symposium. St. Louis, MO. A symposium honoring the lifetime achievements of Dr. Gordon Cragg of the National Cancer Institute, presented by the William L. Brown Center for Plant Genetic Resources. Web site: www.wlbcenter.org. Phone: 314-577-9565. E-mail: bruce.ponman@mobot.org.

November 10-12: CAMEXPO West. Los Angeles, CA. The CAMEXPO conference program features the latest trends, research, clinical trials, and protocols in the field of complementary and integrative healthcare, and the exhibition presents buyers of natural healthcare products and services with a dedicated, focused marketplace. For more information visit the Web site: www.camexpowest.com.

November 16: Herbal Protocols for the Hypothalamic Pituitary Adrenal Axis (HPA) Deficiency & Stress. Washington, NJ. This class will examine the types of herbs (nervines, anxiolytics, adaptogens) useful for relieving stress and promoting HPA axis re-regulation. Contact: Cathy Garland, Herbalist & Alchemist, Inc., 908-689-9020 ext. 101. E-mail: cathy@herbalist-alchemist.com. Web site: www.herbalist-alchemist.com.

November 17-19: Aromatherapy Conference Tours. Santa Monica, CA. Aromatherapy Conference Tours (ACT) is a consortium of medical professionals participating in national educational aromatherapy conferences and free trade shows open to the public in select venues across the country. Each event features expert speakers as well as open panel discussions and hands-on learning workshops over a 3-day weekend. Reservations must be made by October 26, 2006 to receive conference rate of $189. Web site: www.aromatherapyconferencetours.com.

November 20-24: FAPRONATURA 2006. Varadero Beach, Cuba. The Cuban Society of Pharmacology invites you to participate in its First International Symposium on Pharmacology of Natural Products and the First International Symposium of the Latin-American and Caribbean Bulletin of Aromatic and Medicinal Plants. Web site in Spanish: http://www.scf.sld.cu/natprod/portada.htm. Web site in English: http://www.scf.sld.cu/natprod/en/portada-en.htm. Works presented in FAPRONATURA 2006 will be published by PharmacologyOnline journal as "short communications." To see the Author's Guidelines of this journal, visit the Web site: http://www.pharmacologyonline.unisa.it/submissionrules.asp.

November 27—December 2: Applying Functional Medicine in Clinical Practice. Fort Lauderdale, FL. Spend a week with leading experts on functional medicine, the science-based healthcare approach that assesses and treats underlying causes of illness through individually tailored therapies to restore health and improve function. Learn the techniques and take home the clinical tools that will make functional medicine a reality in your practice. For more information, visit the Web site: http://www.functionalmedicine.org/eduprog/afmcp.asp or contact Client Services at 800-228-0622. Early bird cut-off date: October 13, 2006.

November 30—December 3: NNFA SOHO Expo: Orlando, FL. Join industry members from all over the nation and world for this natural products industry trade show and convention. Show combines education programs for businesses with exhibits featuring outstanding products. A golf tournament opens the show on Thursday. Seminars are Thursday-Sunday. Exhibits are open Saturday and Sunday. For more information visit the Web site: www.nnfase.org.

November 30–December 2: First Ibero-American Congress on Phytotherapy [Primer Congreso Iberoamericano de Fitoterapia]. Mexico City. The conference is being sponsored by the Mexican Social Security Institute and the Ibero-American Program for the Development of Science and Technology (CYTED), with the collaboration of the following phytotherapy associations: the European Society for Medicinal Plant Research (GA), Spanish Society for Phytotherapy (SEFIT), European Scientific Cooperative on Phytotherapy (ESCOP), SPFito (Portugal), Argentinian Association of Phytomedicine, and the Brazilian Institute of Medicinal Plants. A pre-conference phytotherapy course will be held from November 27-29. More information (in Spanish) available at the Web site: http://www.fitoterapia.net/congreso/congreso.html.

December 1-5: First International Meeting on Cassava Plant Breeding and Biotechnology. Brasilia, Brazil. The theme of this meeting is cassava enhancement to improve livelihoods in sub-Saharan Africa and northeastern Brazil. Sessions include: wild species and landraces to enhance nutritional content; management of reproduction and propagation systems; biotechnology rools and methods for breeding the crop; and conservation of Manihot genetic resources. Organized by Dr. Nagib Nassar of the University of Brasilia. E-mail: nagnassa@rudah.com.br. Web site: http://www.geneconserve.pro.br/meeting/.

More calendar listings at
www.HerbalGram.org

In this department of *HerbalGram*, we list resources such as publications, organizations, seminars, and networking for our readers. A listing in this section does not constitute any endorsement or approval by *HerbalGram*, ABC, or its Advisory Board.

Biodiversity Conservation Handbook, released in June 2006 from the Environmental Law Institute, an independent environmental education and resource center. The 648-page handbook focuses on biodiversity's background and preservation, explores tools for implementing biodiversity programs in the US, encourages state and local policymakers to "think locally and act globally," and examines ways in which citizens can minimize ecological harm from pollution, land development, and climate change. More information at www.eli.org.

Honest Nutrition, new personal blog of nutritionist Neil E. Levin, available at www.honestnutrition.com. Entries discuss natural health, health freedom, nutrition, dietary supplements, and related topics. Blog designed as third-party reference for retailers or consumers. Site also includes links to previously published articles and letters to the editor by Levin, who is president of Nutrition for Optimal Health Association and nutrition education manager of NOW Foods, a manufacturer of dietary supplements sold in the natural food trade.

CIMER Web site now available in Chinese. The MD Anderson Cancer Center has implemented a Chinese version of the top-level pages of its Complementary and Integrative Medicine Education Resources (CIMER) Web site. A resource for healthcare professionals, patients, and caregivers on safely incorporating complementary and integrative medicine with conventional cancer care. Contains scientifically-based reviews of programs and an award-winning series on discussing complementary therapies with patients. Available at www.mdanderson.org/cimer.

Bulletin of Cannabis Reform, independent public forum launched in August 2006 on DrugScience.org. Discusses marijuana policy, efforts toward policy reform, and approaches to achieve legalization of marijuana for medical purposes. Premier issue features articles about the first modern US patient to receive legal cannabis and information on congressional voting and amendments regarding cannabis. Available at http://www.drugscience.org/bcr/index.html.

Integrative Medicine Updates (IMU), recently launched newsletter of the Health Integrative Medicine Program of the University of Wisconsin. Distributed to clinicians 3 times a year, IMU explores influences of physical and non-physical healing methods for diseases and ailments. Each issue focuses on 1 health topic, such as diabetes or anti-inflammatory diets. Offers tips and information to prevent or treat disease through nutrition-food, mind-body, and exercise interventions. The program's integrative approach seeks to help patients in the least invasive, toxic, or costly ways. Standard Processing Inc., an established manufacturer of unique dietary supplements, funds publication of the free newsletter. To request, e-mail IGNews@hosp.wisc.edu.

Employment

Family owned medicinal herb company seeks highly skilled, compassionate Manager of our Herbal Department. We have been experiencing consistent growth and want someone who desires to share in our vision. The ideal candidate must be an active listener and able to take direction from our founders.

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- Manufacture of Herbal Medicine
- Research Skills
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If you are intuitively motivated, environmentally aware, and committed to a healthy lifestyle we would like to speak with you.

Please email your resume with salary requirements to scott@blessedherbs.com

We are located in Oakham, MA.

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 studies, and medicinal plant reviews. 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 2 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. E-mail 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.

Other

BUSINESS FOR SALE Beautiful retail herb store for sale in the heart of the Northern Rocky Mountains. In business 10+ years. Work for yourself and love what you do! Send inquires to P.F. PO Box 7002 Missoula, MT 59807 or email herbbiz@montana.com.

Get Certified with ABC's Herbal Information Course. This self-paced online course is designed to help retail employees and multi-level distributors communicate knowledgably with customers about herbs and dietary supplements. After successfully completing the course, you'll receive an Herbal Information Specialist Certificate and a window decal announcing "Herbal Information Specialist On Staff." Renewable annually. $69.95 Bulk pricing available. www.herbtraining.com.

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ECHINACEA

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et al; or most likely, it would be different from both of these.

From a commercial and market perspective, the suggested revisions and reclassification of the species in the genus *Echinacea* would obviously require an eventual re-labeling of the commercial *Echinacea* products, a cost that will be of dubious value to the industry and which will no doubt produce added confusion to the consumer. Although such practical commercial considerations are not a basis for supporting or refuting the progress of basic science and the taxonomic interpretations that may ensue, it is of obvious importance to the vast majority of those who trade in those commercially viable species of this popular genus (e.g., *E. angustifolia, E. pallida, and E. purpurea*). Dr. Baum et al are to be congratulated for the quality of their investigations. The question is whether their proposal should become officially accepted by science and then industry. HG

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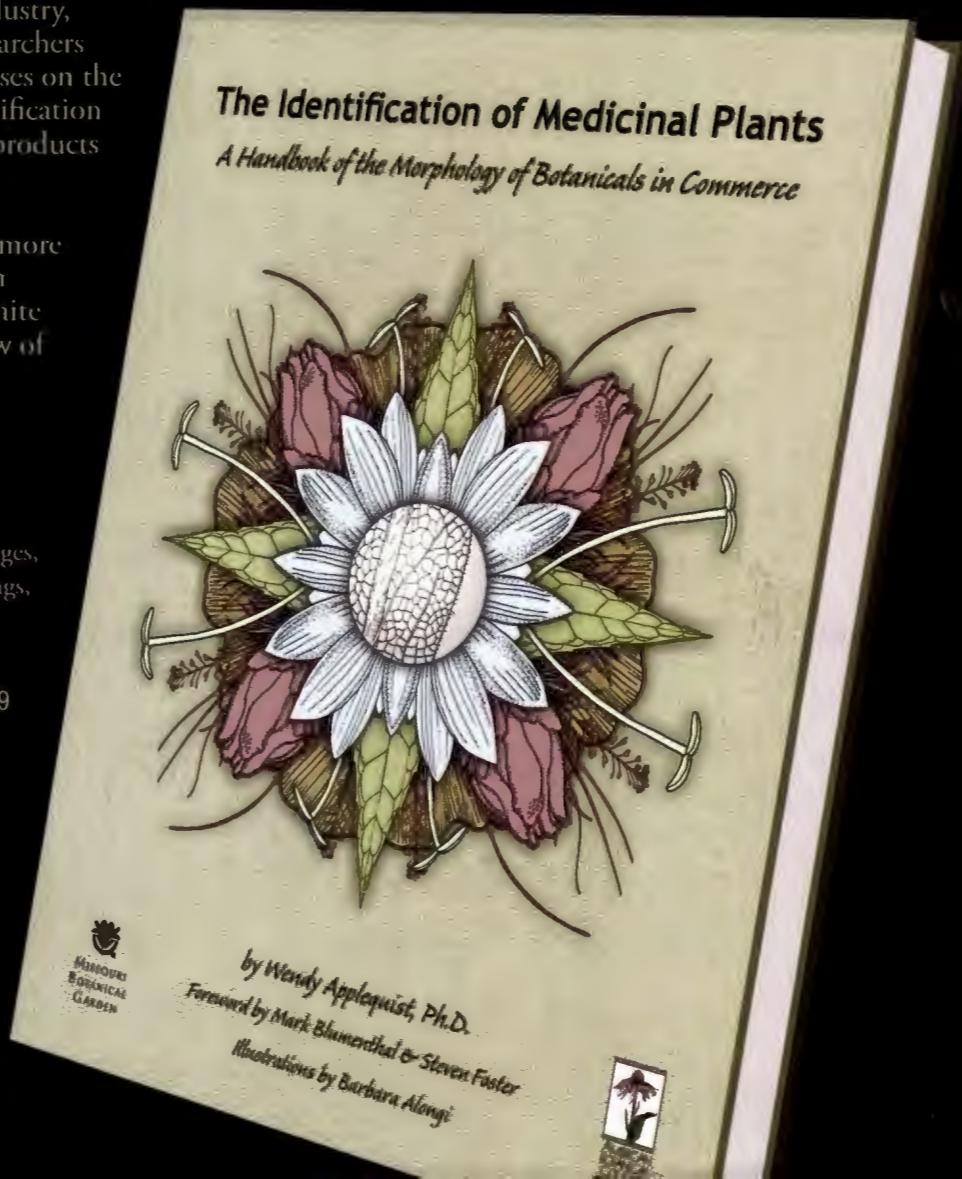

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