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Holy Basil

***Ocimum tenuiflorum* (syn. *O. sanctum*)**

Family: Lamiaceae (formerly Labiatae)

INTRODUCTION

Holy basil is a perennial or annual in the mint family that exhibits the square stem and volatile oils characteristic of its family.[1] It is erect, very branched, strongly aromatic, and mildly hairy.[2] Holy basil is native to India and parts of northern and eastern Africa, Hainan Island, and Taiwan, and grows wild throughout India and up to an altitude of 5,900 feet (1,800 meters) in the Himalayas.[3-5] In China, it occurs in dry, sandy areas of Hainan and Sichuan, as well as in Cambodia, Indonesia, Laos, Malaysia, Myanmar, the Philippines, Thailand, and Vietnam.[6] Holy basil is cultivated in Southeast Asia and also grows abundantly in Australia, West Africa, and some Arab countries.[1,3] In India, the dried leaf, dried seed, and dried whole plant are used separately in the traditional medicine systems of Ayurveda, Siddha, and Unani, as well as in Indian folk medicine. The materials of commerce are obtained mainly from cultivated sources throughout India.[7]

HISTORY AND CULTURAL SIGNIFICANCE

The genus name, *Ocimum*, means "fragrant lipped," and the species name, *tenuiflorum*, means "slender" or "small flowers." In India, *O. tenuiflorum* is known by a variety of names, including: *tulasi*, *ajaka*, *ramatulasi*, and *vriddhatulasi* in Sanskrit; *tulsi*, *baranda*, *kalatulsi*, and *vranda* in Hindi; *tulsi*, *tulshi*, *kalatulsi*, and *kural* in Bengali; *tulsi*, *tulasi*, and *talasi* in Gujarati; *tulasi*, *kalatulasi*, *karitulasi*, *sritulasi*, and *vishnutulasi* in Kannada; *tulsi* in Konkani; *tulasi*, *krishnatulasi*, and *trittavu* in Malayam; *tulasa* and *tulasichajadha* in Marathi; *tulsi* and *bantulsi* in Punjabi; *tulasi* in Tamil; and *tulasi* and *krishnatulasi* in Telegu.[2,4,8] In some circles, the previous Latin binomial, *O. sanctum*, is still preferred, as *sanctum* refers to the historical "holy" status of the plant. Sorting out the species that are referred to as holy basil can be confusing. *Ocimum tenuiflorum* has at least two varieties: *Krishna* or *Shyama Tulsi* (dark green-to-purple-leaved) and *Sri* or *Rama Tulsi* (green-leaved).[4,9] A third variety, *Kapoor* (or *Kapur*) *Tulsi* (also green-leaved), may or may not be *O. tenuiflorum*; some sources surmise that it is *O. kilimandscharicum*, native to East Africa.[10,11] A separate species, *O. gratissimum* ("very grateful basil" or "pleasing basil"), is known as *Forest* or *Vana Tulsi*. Even though it is a different species, *O. gratissimum* also is considered sacred in India and is used in the same ways as the *O. tenuiflorum* varieties.[2]

Tulsi is one of the principal herbs used in the Ayurvedic medicine system, in which it is known alternately as "The Queen of Herbs," "The Incomparable One," and "The Mother Medicine of Nature."[9] It holds a supreme place in the ancient Vedic scriptures and is integrated into daily life by Hindus through religious worship. Hindu homes typically have a tulsi plant growing in an earthen pot in or around the home. In Ayurveda, it is believed that the best

Holy Basil *Ocimum tenuiflorum*. Photo ©2013 Steven Foster

way to take tulsi medicinally is in its raw, fresh, whole form as a hot-water infusion.[9]

Tulsi is combined with various other herbs in Ayurvedic preparations to treat the following conditions and symptoms: abscesses, abdominal pain, teething-related ailments, anemia, arthritis, boils, bronchial asthma, bronchitis, catarrh (respiratory tract inflammation), constipation, coryza (cold), cough, diarrhea due to giardiasis or amebiasis (both caused by microscopic parasites), dysentery, eye diseases (topically), headaches, fever (including chronic and malarial fevers), filariasis (a parasitic disease caused by nematodes), general debility or weakness, goiter, gonorrhea, hernias, intestinal worms, jaundice, leucoderma (loss of skin pigmentation; applied topically), loose teeth (as a snuff or mouth lotion), loss of appetite, lumbago (low back pain), memory enhancement, piles (inflamed hemorrhoids), premature aging and graying of hair, pulmonary tuberculosis, rheumatism, ringworm (topically), syphilis, thinness of semen, strangury (painful, frequent urination in small volume), tubercular lymph nodes, tubercular leprosy, and tumors.[2,9,12]


Holy Basil *Ocimum tenuiflorum*. Photo ©2013 Steven Foster

Ayurvedic medicine also has credited holy basil with numerous actions, including the following: adaptogenic, antibacterial, antiperiodic (prevents the recurrence of disease symptoms), antipyretic/febrifuge (reduces fever), antiseptic, antispasmodic, carminative (relieves intestinal gas), diaphoretic (promotes sweating), expectorant, nervine, and stimulant.[2,9,12,13]

There are *O. tenuiflorum* standards monographs published in the *Ayurvedic Pharmacopoeia of India* (Vol. II, 1999, and Vol. IV, 2004) and *Unani Pharmacopoeia of India* (Vol. V, 2008), as well as *Thai Herbal Pharmacopoeia* (Vol. I, 1995), *Vietnamese Pharmacopoeia* (1st ed., 1983), and World Health Organization (WHO) Monographs (Vol. 2, 2002).[2] The WHO monograph lists other uses that are described in pharmacopeias and in traditional systems of medicine including treatment of arthritis, asthma, bronchitis, common cold, diabetes, fever, influenza, peptic ulcer, and rheumatism.[3]

CURRENT AUTHORIZED USES IN COSMETICS, FOODS, AND MEDICINES

In countries where the Ayurvedic system of medicine is recognized and practiced (*e.g.*, India, Bangladesh, Bhutan, Malaysia, Nepal, and Sri Lanka), the powdered, dried leaf of holy basil is used therapeutically, depending on the formulation, for treating the following conditions: acute rhinitis (inflammation of the mucous membrane of the nose), asthma or dyspnea (shortness of breath), hiccups, cough, tastelessness (inability to differentiate tastes, which may be due to improper digestion or lack of desire for food), worm infestation, skin diseases, intercostal neuralgia (pain in the tissue between the ribs), and pleurodynia (pain in the upper chest [pleural cavity]). Similarly, the dried whole plant (prepared in juice form) is used to treat asthma or dyspnea, hiccups, cough, worm infestation, and skin diseases, as well as pleurisy, calculi (stones), vomiting, and eye diseases.[14]

The powdered seed also is used, depending on the formulation in which it occurs, for treatment of acute rhinitis, asthma or dyspnea, hiccups, cough, skin diseases, tastelessness, intercostal neuralgia and pleurodynina, as well as inflammation, intestinal helminths (worm-like parasites), dysuria or painful urination, foul smell, artificial poisons, hematological diseases, and parasitic infections.[15]

In countries where the Unani system of medicine is recognized and practiced (*e.g.,* Bangladesh, India, Malaysia, Pakistan, and Sri Lanka), holy basil (*rehan*) leaf and whole plant are used therapeutically (in dried or juice forms) to treat amenorrhea, cough, palpitation, and weakness of the stomach.[16]

In Canada, holy basil leaf and seed are classified as active ingredients of licensed natural health products (NHPs) that require pre-marketing authorization from the Natural Health Products Directorate (NHPD) and must be manufactured in compliance with NHP good manufacturing practices (GMPs). Authorized uses for holy basil leaf preparations (powdered leaf, decoctions, infusions, and non-standardized aqueous extracts) outlined in the NHPD compendial monograph include "traditionally used in Ayurveda (as an expectorant and/or demulcent) to help relieve cough (*Kasa*) and colds," "traditionally used in Ayurveda (as an expectorant) to help relieve respiratory catarrh," "traditionally used in Ayurveda as a cardiotonic (*Hrdya*)," and "traditionally used in Ayurveda to aid digestion (*Dipani*) and stimulate appetite (stomachic)."[17]

The powdered dried seed may be labeled and marketed in Canada for the following uses: "traditionally used in Ayurveda (as a demulcent) to help relieve cough (*Kasa*)," "traditionally used in Ayurveda as a cardiotonic (*Hrdya*)," and "traditionally used in Ayurveda to aid digestion (*Dipani*)."[18]

In the United States, holy basil is not listed as Generally Recognized as Safe (GRAS) in the Code of Federal Regulations (CFR) for use in conventional food products, nor does holy basil appear in the US Food and Drug Administration's (FDA) GRAS Notice Inventory database. Holy basil plant parts are permitted, however, as dietary supplement components that require FDA notification within 30 days of marketing a product (if a "structure-function" claim is made), and the product must be manufactured according to dietary supplement GMPs. In 2012, the United States Pharmacopeial Convention (USP) published proposed dietary supplement quality standards monographs for "Holy Basil" (dried leaf) and "Powdered Holy Basil" (pulverized dried leaf) containing no less than 0.5% triterpenes, calculated as the sum of oleanolic acid and ursolic acid, and a corresponding "Powdered Holy Basil Extract" monograph for public consultation and finalization in 2013. The new USP monographs will be acceptable for use as holy basil leaf dietary supplement component specifications.[19]

Concerning use of holy basil in cosmetic products, the European Commission Health and Consumers Directorate lists "Ocimum Tenuiflorum Extract" for skin-conditioning functions, and "Ocimum Tenuiflorum Oil" (wax obtained from the leaves of *O. tenuiflorum*) for emollient (softens and smooths the skin), hair-conditioning, and skin-conditioning functions.[20]

MODERN RESEARCH

Holy basil contains alkaloids, carbohydrates, fats, glycosides, phenols, proteins, saponins, tannins, and terpenes.[9] Pharmacological and *in vitro* laboratory studies have exhibited adaptogenic, anabolic, anti-asthmatic, antidiabetic, antidiarrheal, anti-inflammatory, antioxidant, antipyretic, anti-radiation, anti-stress, calming, cardiac depressant, contraceptive, hepatoprotective, hypotensive, immunomodulatory, neuro- and cardio-protective, and mosquito-repelling properties for the plant.[9,13]

Tulsi is believed to increase immunity when taken on an empty stomach. In a 2011 double-blind, randomized, controlled trial, 24 healthy volunteers consumed 300 mg capsules of holy basil leaves (70% ethanolic extract; Dabur Pharmaceutical Ltd., Ghaziabad, India) or placebo on empty stomachs every day for four weeks, followed by a three-week washout period before crossover to the next intervention. The holy basil group had significantly increased levels of IFN-γ, IL-4, and percentages of T-helper cells and natural killer (NK) cells, showing holy basil's immunomodulatory effects in humans.[21]

Two double-blind pilot studies in 2009 investigated holy basil and four other Ayurvedic herbs for their reputed immune-enhancing effect.[22] The first study included 32 volunteers randomized to two treatment groups of 16 each who consumed three cups daily (over the course of two months) of regular tea or Natural Care tea (Hindustan Unilever Research Center, Bangalore, India), which contains holy basil (0.5%); ashwagandha (*Withania somnifera*, Solanaceae, 0.5%); licorice (*Glycyrrhiza glabra*, Fabaceae, 0.5%); ginger (*Zingiber officinale*, Zingiberaceae, 1.5%); and cardamom (*Elettaria cardmomum*, Zingiberaceae, 1.5%). NK cell activity was measured after one and two months of tea consumption. While there were no significant changes in either group at the end of the first month, NK cell activity significantly increased after two months in the Natural Care tea drinkers but not in the regular tea group.

The second study was a larger, double-blind, crossover study in which 110 subjects (60 male, 40 female [sic]) were assigned randomly to two groups.[22] Each group consumed three cups of tea (Natural Care or regular [*Camellia sinensis*, Theaceae]) per day for two months. NK cell activity was measured before a 15-day washout period when no tea was drunk. The groups then switched to the other tea for another two months, after which NK cell activity was measured again. NK cell activity increased in both groups after two months, but the increase in the Natural Care tea drinking groups was approximately 4.2 times higher, while the NK cell activity in the regular tea group was about 2.9 times higher.

Holy basil was investigated for its effect on generalized anxiety disorder (GAD) in a 2008 study.[23] The study was conducted on 35 patients suffering from GAD from the outpatient clinics of the J. B. Roy State Ayurvedic Medical College and Hospital in Calcutta, India. Each subject was given 500 mg holy basil (70% ethanol extraction repeated three times, reduced in a rotary evaporator, then freeze-dried and packaged in gelatin capsules; manufacturer not stated) orally twice daily after a meal for 60 days. Baseline score index was 84.42±7.56 at the start, decreased to 68.17±7.84 (-19.2%) at 30 days, and 55.54±7.20 (-34.2%) at 60 days. Stress index at baseline was 95.65±8.42 and decreased to 84.32±9.08 (-11.5%) at 30 days and 68.45±9.60 (-27.5%) at 60 days. Additionally, depression index declined from 66.45±5.68 at baseline to 57.65±5.04 (-13.2%) at 30 days and 45.97±6.27 (30.8%) at 60 days.

A 2001 open, prospective, multicenter clinical study investigated the efficacy of an herbal eye drop containing holy basil on various ophthalmic conditions.[24] Ophthacare® is an aqueous extract of six plants and honey made by Himalaya Drug Co. (Makali, Bangalore, India). Ophthacare comprises 0.60% w/v ajowan seed (*Trachyspermum ammi*, syn. *Carum copticum*, Apiaceae); 0.65% w/v belleric myrobalan fruit (*Terminalia bellerica*, Combretaceae); 1.30% w/v amla (*Phyllanthus emblica*, syn. *Emblica officinalis*, Euphorbiaceae); 1.30% w/v turmeric rhizome (*Curcuma longa*, Zingiberaceae); 1.30% w/v holy basil leaf; 1.10% w/v damask rose petals (*Rosa damascena*, Rosaceae); 0.5% w/v camphor crystal (*Cinnamomum camphora*, Lauraceae);

and 3.70% w/v honey. Eye drops were applied at the rate of two drops four times daily for 15 days on 100 patients with acute conjunctivitis (allergic, bacterial, or viral) (n=35), acute dacryocystitis (inflammation of the nasolacrimal sac) (n=20), conjunctival xerosis (dry eye) (n=7), degenerative conditions such as pterygium/pinguecula (n=15), or who were postoperative cataract patients (n=23). Therapeutic responses occurred in most of the patients with the postoperative cataract patients experiencing the most benefit (95%), followed by dacryocystitis patients (88.2%), acute conjunctivitis patients (87.5%), patients with degenerative conditions (76.9%), and conjunctival xerosis patients (66.7%).

In a 1996 randomized, single-blind, placebo-controlled, crossover study, 40 type 2 diabetes patients were randomized to consume holy basil leaf tea for four weeks followed by placebo leaf tea for four weeks or the reverse after a five-day run-in period in which they all consumed holy basil leaf tea.[25] The authors concluded that consumption of the holy basil tea resulted in significant reduction in fasting blood sugar and postprandial blood sugar, as well as a moderate reduction in cholesterol. However, the Jadad score for this study was 1 (on a scale of 0 [very poor] to 5 [rigorous]), suggesting lack of adequate design and controls and that further studies are necessary.

A number of clinical studies were reported in the late 1900s, including ones for treatment of bronchial asthma, viral encephalitis, stress-related arterial hypertension, cell-mediated and humoral immune response, and chronic fatigue.[9] While these studies suggested some positive benefit for the conditions studied, they were all small pilot studies.

FUTURE OUTLOOK

Of the estimated 960 medicinal plant species that form the source of 1,289 botanical raw drugs traded in India, *O. tenuiflorum* is among the top 117 species whose annual domestic consumption exceeds 100 metric tons (MT). Ranking sixth in terms of volume, Indian domestic consumption of holy basil is estimated at 3,533 MT. In terms of trade volume and consumption, annual demand was estimated to be between 2,000 to 5,000 MT in 2008. Most of the commercial supply is produced through cultivation.[26]

Demand for holy basil with sustainability certifications (*e.g.*, organically grown, biodynamic, and/or fair trade) appears to be increasing, evidenced by the fact that Indian farms are beginning to implement both ecological and social standards for the growing export market, and US companies are investing in the marketing of ecological and socially responsible certified tulsi products. Two such examples are the Phalada Agro Research Foundation Pvt. Ltd. (Bangalore, India) and the Putharjhora Tea Garden Pvt. Ltd. (Calcutta, West Bengal, India).

On the American side of the trade, Honest Tea (Bethesda, MD) has worked closely with Fair Trade USA (Oakland, CA) to help the Organic Tulsi Farm, part of the Phalada cooperative of 750 farms, obtain Fair Trade certification.[27] Phalada's tulsi producer group and processing unit also hold Fair For Life Social and FairTrade Certification issued by the Institute for Market Ecology (IMO), as well as biodynamic certification from Demeter International.[28,29]

Another US company, Davidson's Organics (Sparks, NV), now markets certified fair trade, biodynamic, and organic tulsi leaf teas grown by certified operator Putharjhora Tea Garden Pvt. Ltd.[30]

Other big players in the marketing of sustainable tulsi teas in North America include Choice Organic Teas (Seattle, WA), which specializes in fair trade, organic, and Non-GMO-Project Verified teas; Pukka Herbs Ltd. (Bristol, UK), which specializes in fair trade, FairWild®, and organic teas; and Organic India® (Boulder, CO). Organic India has decided not to pursue fair trade certification at this time, but states that its labor and trade practices go above and beyond what any certification requires, *i.e.*, they provide their tulsi farmers and their families with health care, education, and a sustainable method of agriculture.[31]

Presently, in the Canadian market, there are 50 licensed NHPs that contain holy basil leaf, leaf extract, or seed as active ingredients, including, for example, Holy Basil 500 mg Vegetarian Capsules (Organika Health Products Inc.), Holy Basil Tea (St. Francis Herb Farm, Inc.), Perfect Calm® tablets, Wholemega® Focus capsules, and Zyflamend® P.M. capsules (New Chapter Inc.).[32] HG

—Gayle Engels and Josef Brinckmann

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dear *reader*

Adulteration of Black Cohosh

From the moment we envisioned the establishment of the ABC-AHP-NCNPR Botanical Adulterants Program more than two years ago, black cohosh was included on the list of herbs for which we had a confirmed basis for adulteration. Two published analytical papers by ABC Advisory Board member Professor Ed Kennelly at Lehman College at the City University of New York and his colleagues detected chemical marker compounds characteristic of several widely suspected adulterant species from China, *i.e,*. other species in the genus *Actaea*. The American Herbal Products Association also has included black cohosh in its list of "Known Adulterants."

In this issue, we present author and botanical photographer Steven Foster's extensive review of the confusing nomenclature associated with the genus *Actaea* (syn. *Cimicifuga*), of which *Actaea racemosa* (syn. *Cimicifuga racemosa*) — known most commonly as black cohosh in North American and many English-speaking countries) — is the only species that is legally permitted to be sold as "black cohosh" in the United States.

Black cohosh is used primarily to help middle-aged and older women manage symptoms associated with menopause. In the United States and elsewhere, black cohosh dietary supplements are self-selected by many women for such use, which is supported by a variety of published clinical trials. Also, in what appears to be increasing frequency, black cohosh preparations are being recommended by a growing body of licensed healthcare practitioners.

Consumers and practitioners need to be certain that the "black cohosh" root material (or its extract) in the capsules or tablets in their bottles of dietary supplements really are what the labels purport them to be. While there are numerous responsible companies that produce high-quality, properly authenticated black cohosh products, there are some companies whose quality control programs are apparently inadequate, hence the detection of adulterants in some commercial products. It is past time for *all* members of the herb and dietary supplement industry in the United States, and the botanical products industry around the world, to institute and adhere to appropriate quality control measures related to properly identifying and authenticating black cohosh products, as well as all herbal products.

With increased awareness of these problems associated with accidental and intentional adulteration of black cohosh, the old excuse used by some manufacturers — "We didn't know to test for an adulterant in black cohosh" — and related excuses won't fly anymore. It's time to stop the errors caused by inadequate identity testing and the possible intentional substitution of cheaper Chinese materials in order to ensure that consumers get what they want and what they think they're buying.

This article is the latest in a series that ABC is publishing as part of the ABC-AHP-NCNPR Botanical Adulterants Program, in which ABC is partnering with our good friends at the American Herbal Pharmacopoeia and the National Center for Natural Products Research at the University of Mississippi. Previous articles in this series include Foster's excellent historical review of botanical adulteration (*HerbalGram* 92), his article on adulteration of skullcap with germander (*HerbalGram* 93), John Cardellina's review of analyses showing that many materials labeled "grapefruit seed extract" are adulterated with synthetic industrial disinfectants (*HerbalGram* 94), and Foster's article on the adulteration of bilberry extract with various synthetic and natural materials (*HerbalGram* 96).

To date, the Botanical Adulterants Program is endorsed by more than 100 members of the international herb industry, third-party analytical laboratories, professional and trade organizations, media members, accredited schools of natural medicine, and many more.

Also, of course, as is customary with articles in our adulterants series, this article has been peer reviewed extensively and carefully for accuracy by numerous highly qualified experts in the fields of botany and taxonomy, chemistry and analytics, and the industrial trade of authentic North American black cohosh raw materials.

Mark Blumenthal

ABC Advisory Board

Each issue of *HerbalGram* is peer reviewed by members of the ABC Advisory Board and other qualified experts before publication.

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On the Cover
Black Cohosh *Actaea racemosa.*
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ABC Celebrates Employee of 25 Years, Margaret Wright

Margaret Wright began working as a part-time employee for Bee Creek Botanicals, a company established by American Botanical Council (ABC) Founder and Executive Director Mark Blumenthal, in January of 1988. Shortly thereafter, in November of that year, she transitioned to the newly established ABC, where she has worked full-time ever since — with 17 co-workers — a departure from the more modest and upstart atmosphere she first encountered.

"Back then, there were three people in the office: Mark, who did his usual stuff except he didn't travel nearly as much as he does now; his secretary, Mary, who did sales calls for Bee Creek, payroll, and tried to keep Mark on track; and me, who did everything else," Margaret wrote in 2000, in her reflection "Back in Time with ABC." "Mark would come into my office every day," she wrote, "and ask if I still liked it here."

In "Back in Time with ABC," Margaret recalls those early days with fondness. "We had fun," she said. "For our first Thanksgiving and holiday parties, we could all fit around the kitchen table. We would go out to lunch for people's birthdays and all sit at one small table. We even went to a movie one time together after work."

Margaret Wright next to a memorial tree planted in memory of her mother, Muriel Goddard Hull. ©2013 ABC

Over the course of 25 years, Margaret traveled to Costa Rica through an ABC program and witnessed the organization's numerous technological upgrades, such as ABC's first fax machine. "We were all so excited," she said with a laugh. She also became ABC's official, much-lauded birthday-cake baker. ABC employees look forward to monthly staff meetings as they almost always are coupled with a sumptuous dessert from Margaret to celebrate corresponding staff birthdays. Popular options include her chocolate silk pie, fudge, and of course her infamous and dangerously delicious carrot cake — Mark's personal favorite — which is in fact so good it has been known to convert carrot-cake detractors.

ABC's work-culture values have remained consistent since '88. For Margaret, who had three children under the age of four when she joined ABC, part of the appeal of the organization was that it honored the importance of family above all. "One of the things that I liked about ABC in the beginning, and I started out working there when my kids were very young… it was a good place to work for a family person because Mark always believed in putting family first." Margaret's daughter, Carrie, even worked at ABC for a short time. "She was 14, and we didn't have a receptionist that summer for some reason, so she came to work there and was a receptionist, and Mark got a call one time, and whoever it was said 'It sounds like your receptionist is 14,' and he said 'She is!'"

Margaret found friendship at ABC, as well, particularly with finance coordinator Cecelia Thompson, who was hired about six months after Margaret. "We became friends right away, but we weren't in the same office," she said. That situation was remedied when ABC moved to its present location at its historic Case Mill Homestead headquarters.

Before coming to Bee Creek and ABC, Margaret leased and maintained plants for office buildings. Her initial title at ABC was subscription coordinator, and she continued in that role until ABC relocated to Case Mill. She now serves as accounting coordinator, a vocation that provides her with opportunities to engage with interesting people from around the world.

"One of the things I like about my job is I get to talk to people in other states and countries," said Margaret. "Some of them I've been talking to for years and I kind of think of them as my friends. If we're having a particularly hot summer or I've heard that it's snowing extra hard in some community and I am on the phone asking about payment or membership, I'll sometimes ask them about the weather where they are. It's kind of nice."

Another component of the job Margaret enjoys most is sleuthing. "Cecelia and I always say we like to play detectives," she said. "I like solving mysteries. Sometimes I have to figure out a membership that I can't find in our system or a mathematical question that requires a lot of concentration. It's fun when I figure it out."

It comes as no surprise, then, that Margaret is a trusted connoisseur of BBC mystery series — and British television series in general — and her consistently good taste is relied upon by many in the ABC offices. The same can be said in the area of literature as a result of her voracious appetite for books. Among all of her wonderful qualities and skills, Margaret is perhaps most beloved for her cunning, wily, and effortless sense of humor, which she never neglects to bring to work.

"Margaret is every employer's dream," said Blumenthal. "I can never adequately express how much I appreciate and respect her as an employee, and as a person. She is one of the most solidly consistent employees I've ever had in over 40 years of owning or running a business or organization. She's intensely responsible, totally reliable, incredibly loyal, performs her duties virtually flawlessly, handles myriad details effectively, has an excellent 25-year institutional memory, and gets along exceedingly well with the rest of the staff. Who could ask for anything more?"

To the delight of everyone fortunate enough to work alongside her, even after 25 years, Margaret is still going strong at ABC. "Cecelia and I have a pact, and Mark wanted to join in on our pact. He said he's never quitting, so that means we can't, so…." HG

—Ash Lindstrom

ABC Welcomes New Advisory Board Members

The American Botanical Council (ABC) announces the addition of 17 new members to its Advisory Board. These esteemed individuals — with diverse academic backgrounds ranging from analytical chemistry, oncology, and pharmacognosy to environmental science, aromatherapy, and Traditional Chinese Medicine — are committed to promoting healthier living through herbal and plant-based medicine. Advisory Board members volunteer their time to peer review articles that appear in *HerbalGram*, HerbalEGram, HerbClips, and other ABC publications. Additionally, ABC staff and *HerbalGram* editors seek feedback and advice from Advisory Board members on issues such as research questions, article ideas, ABC policies, book reviews, and much more.

The new Advisory Board members include an oncologist, a cardiologist, an endocrinologist, a dermatologist, a nurse/aromatherapist, a nutritionist, a doctor of acupuncture and oriental medicine, a mycologist, a geneticist, two pharmacognosists, two family practice physicians, two natural product chemists, and two environmentalists.

"We are deeply grateful to include these experts on the ABC Advisory Board," said ABC Founder and Executive Director Mark Blumenthal. "For many of these individuals, receiving official ABC Advisory Board status simply formalizes an already established, long-term relationship in which many of these friends and colleagues have been contributing their time and expertise to ABC and many of its publications as expert peer reviewers. The wide spectrum of scientific and clinical expertise held by these individuals as a group reflects the increasing complexity and sophistication of the modern herbal movement and of ABC's vital nonprofit educational mission."

Following are the names and brief bio-sketches of the new ABC Advisory Board members.

Donald I. Abrams, MD, is chief of the Hematology-Oncology Division at San Francisco General Hospital, an integrative oncologist at the University of California – San Francisco (UCSF) Osher Center for Integrative Medicine, and a professor of clinical medicine at UCSF. A graduate of Brown University and Stanford University College of Medicine, Dr. Abrams worked in a UCSF retrovirology laboratory when the first cases of AIDS were being diagnosed. His current research, some of which is supported by grants from the National Institutes of Health (NIH), involves cancer, nutrition, and HIV/AIDS. Dr. Abrams is a member of the American Medical Association, the Society for Integrative Oncology, and a member and past president of the Gay and Lesbian Medical Association. Currently, he is involved with clinical investigations in integrative oncology with specific interests in medicinal mushrooms, cannabis (*Cannabis* spp., Cannabaceae), Traditional Chinese Medicine interventions, and nutrition. He co-edited an Oxford University Press textbook, *Integrative Oncology* (2009), with Andrew Weil, MD, and serves on the editorial boards of the *Journal of AIDS*, *Integrative Medicine Insights*, and as the associate editor of *The Journal of the Society of Integrative Oncology*.

Gary N. Asher, MD, is an assistant professor in the University of North Carolina (UNC) School of Medicine's Department of Family Medicine, medical director of Integrative Medicine Services at UNC's Lineberger Comprehensive Cancer Support Program, and a practitioner of medical acupuncture at UNC's Family Medicine Acupuncture Clinic. A graduate of Columbia University and Ben Gurion University in Israel, Dr. Asher also has a Master of Public Health degree with a focus in health care and prevention from UNC. He has over 15 years of experience working with botanical medicines, including clinical training and practice, and gained manufacturing and quality control experience within the herbal industry during his time as a lab manager for several small companies. His postdoctoral fellowship at UNC included training in complementary and alternative medicine clinical research and clinical pharmacology. Dr. Asher is a member of the Society for Integrative Oncology, the American Academy of Medical Acupuncture, and the American Society for Clinical Pharmacology and Therapeutics. Currently, he is conducting two clinical trials with curcumin, a component of turmeric (*Curcuma longa,* Zingiberaceae).

Robert Alan Bonakdar, MD, has served as the director of pain management at Scripps Center for Integrative Medicine since 2002. Dr. Bonakdar focuses on herbal medicine and natural product therapies in integrative family medicine, particularly for chronic pain conditions. A member of several conventional and integrative medical associations, he likewise serves as a peer reviewer for a variety of medical journals, including *American Family Physician* and the *Journal of Alternative and Complementary Medicine*. He also sits on the boards and committees of several foundations and groups, including his current position as president of the American Academy of Pain Management. Dr. Bonakdar authors and edits many chapters and articles on integrative medicine, and was editor of *The H.E.R.B.A.L. Guide: Dietary Supplement Resources for the Clinician* (Lippincott Williams & Wilkins, 2010). In 2004, he co-founded the renowned Scripps conference "Natural Supplements: An Evidence-Based Update," which he still co-directs.

Nancy Booth, PhD, currently works for Spherix Health Sciences Consulting, a division of ChromaDex, as a senior science consultant. In that role, she counsels clients on product safety and regulation. Her specialties include the areas of dietary supplements, food ingredients, pharmacognosy, analytical method development, chemistry, and biochemistry. Dr. Booth earned her doctorate in pharmacognosy from the esteemed College of Pharmacy at the University of Illinois – Chicago, and conducted her postdoctoral research on botanical dietary supplements through a fellowship from NIH. Dr. Booth is also a member of the American Chemical Society, the Institute for Food Technologists, the American Society of Pharmacognosy, and the Chemical Consultants Network. She is an American College of Nutrition Fellow.

Deni Bown serves as project manager of the International Institute of Tropical Agriculture (IITA) Forest Project in Ibadan, Nigeria. Her responsibilities comprise environmental education, reforestation, natural resource management, and biodiversity monitoring, in addition to the management of IITA's Nursery and Medicinal Plant Garden. Bown is the author of several books, including the Herb Society of America's *Encyclopedia of Herbs & Their Uses* (1995), and has been a recipient of the British Broadcasting Corporation's Wildlife Photographer of the Year award in the plants category. She has chaired the UK's Herb Society, served as regional chair of the UK's Plant Heritage, and was the honorary president of the Herb Society of America. At present, Bown consults for Lagos State Urban Forest in Nigeria.

Jane Buckle, RN, PhD, a registered critical care nurse, specializes in holistic therapies for the nursing profession. Through her consulting firm, R.J. Buckle Associates, LLC, many scholarly journal articles, mainstream media stories, and two aromatherapy books — *Clinical Aromatherapy in Nursing* (Arnold Publishers, 1997) and *Clinical Aromatherapy: Essential Oils in Practice* (Churchill Livingstone, 2003) — Dr. Buckle has taught thousands of nurses and other healthcare practitioners the benefits of integrating essential oils into patient treatment. She created the United States' first clinical aromatherapy course for nurses, has lectured on complementary medicine at the University of West London, and currently serves on the editorial boards of several peer-reviewed journals. In 1994, Dr. Buckle patented her own gentle, structured touch method, known as the "M" Technique. She received her PhD in health service management and a post-doctorate diploma in biostatistics and epidemiology as an NIH-funded Complementary and Alternative Medicine Research Fellow at the University of Pennsylvania.

Alan M. Dattner, MD, is a pioneer in holistic dermatology, a field that integrates nutrition, skin care, and natural products. He has served as a clinical cancer fellow at Albert Einstein College of Medicine, a fellow of the American Academy of Dermatology (AAD), and as a visiting scientist in the dermatology branch of the National Cancer Institute, where he discovered important links between environmental factors and inflammatory diseases. Dr. Dattner graduated from the University of Rochester and obtained his medical degree from New York University, and was a founding member of the AAD's Task Force for Nutrition and the Evaluation of Alternative Medicine. He lectures and writes on holistic dermatology topics, operates a clinical practice in New Rochelle, New York, and also sees patients at the Healthy Tao Center for Wellbeing in Manhattan.

Stefan Gafner, PhD, is the director of analytical chemistry at Tom's of Maine, where he focuses on quality control of botanical raw materials and finished products, as well as plant metabolites with antibacterial and anti-inflammatory properties for applications in oral and personal care. After graduating with a BSc in pharmacy from the University of Bern's Institute of Pharmacy in 1992 and a PhD in pharmaceutical sciences from the University of Lausanne in 1997 — both located in Switzerland — Dr. Gafner moved to the United States for his postdoctoral work on plant-based cancer chemopreventative agents at the University of Illinois – Chicago. Dr. Gafner is a member of the American Society of Pharmacognosy, the Society for Medicinal Plant

Research (GA), and the Phytochemical Society of Europe. He also serves on the editorial board of *Natural Products Against Cancer* and is a reviewer for the *Journal of Natural Products*, *Phytochemistry*, and *Planta Medica*. To date, Dr. Gafner has co-authored more than 30 peer-reviewed publications and book chapters and has been awarded three patents.

Frank L. Greenway, MD, is the medical director and a professor at Louisiana State University's (LSU) Pennington Biomedical Research Center, a clinical professor of medicine in the Department of Medicine at the State University Medical Center in New Orleans, and an adjunct professor in LSU's Human Ecology Department. Dr. Greenway is a graduate of the University of California – Los Angeles School of Medicine and Stanford University, and served as a major in the US Army National Guard's Medical Corps. He is currently a member of the International Association for the Study of Obesity, the American Society for Nutritional Sciences, and the American Association of Clinical Endocrinologists. Dr. Greenway's current research involves health outcomes of weight loss, diabetes prevention, resveratrol treatment for insulin sensitivity, and vitamin D for type 2 diabetes. He has authored more than 150 articles in peer-reviewed journals.

Mimi Guarneri, MD, founded the Scripps Center for Integrative Medicine in La Jolla, California, where she served as medical director from 1999 to 2012 and thereon as senior consultant in integrative medicine. Dr. Guarneri — who is board-certified in cardiology, holistic medicine, internal medicine, and nuclear medicine — earned her doctoral degree from the State University of New York Downstate Medical Center in Brooklyn. Currently, Dr. Guarneri is an assistant clinical professor in the Department of Medicine at the University of California – San Diego, as well as director of the Integrative Cardiology Fellowship at Scripps Center for Integrative Medicine and Department of Cardiology. Her articles have appeared in respected journals, including *Annals of Internal Medicine* and the *Journal of Echocardiography*.

Susan Leopold, PhD, is executive director of the medicinal plant conservation nonprofit United Plant Savers (UpS). She manages all UpS programs, including the Botanical Sanctuary Network, Partners in Education, UpS membership and internships, garden grants, and the at-risk plant program. She earned her PhD in environmental studies at Antioch University – New England, for which she completed her dissertation titled "Loss of Ethnobotanical Knowledge in the Bull Run Mountains." For the seven years preceding her employment at UpS, Dr. Leopold was a librarian at the renowned Oak Spring Garden Library, home to — among other treasures — the collection of rare botanical books and manuscripts of Rachel Lambert Mellon. There, Dr. Leopold entered the collection into a searchable database, established a digital photography lab, and oversaw graduate research.

Rachel Mata, PhD, is a professor at the Universidad Nacional Autónoma de México. Her research interests include natural product drug and agrochemical discovery and chemistry, biochemistry, and pharmacology of medicinal plants. Among her 180 scientific publications to date, Dr. Mata has authored a number of book chapters and respected journal articles as well as three books. She is a member of the editorial boards of the *Journal of Natural Products* and *Current Topics in Medicinal Chemistry*, and she co-edited the book *Phytochemistry of Medicinal Plants* (Springer, 1995). She studied for her MSc and PhD in medicinal chemistry at Purdue University in Indiana. She also held a teaching position at Universidad Central de Venezuela, where she earned her bachelor's degree in pharmacy.

William Morris, PhD, DAOM, LAc, president of the Academy of Oriental Medicine at Austin's (AOMA) Graduate School of Integrative Medicine, is a leading figure within North America's Traditional Chinese Medicine community. Morris led the American Association of Acupuncture and Oriental Medicine to become a single national association, and later played an instrumental role in AOMA's obtaining regional accreditation with the Southern Association of Colleges and Schools as a level 5 doctoral granting institution. Prior to that, he spent more than a decade of study examining the Ding family lineage of internal medicine and the Gu family lineage of external medicine. He earned a doctorate in acupuncture and oriental medicine, a PhD in transformative studies, and a Master of Science in medical education. Morris has written several books on acupuncture and Chinese medicine — including *Mai Dao: Path of the Pulse* (2009) and *Li Shi-Zhen Pulse Studies: An Illustrated Guide* (People's Medical Publishing House, 2011). He serves as editor and regularly authors articles for *Acupuncture Today* and *American Acupuncturist*, and lectures on pulse diagnosis, Chinese herbs, and other topics.

Danica Taylor Harbaugh Reynaud, PhD, is the founder and CEO of AuthenTechnologies LLC, the founder and executive director of the nonprofit International Sandalwood Foundation, and a visiting scholar and museum specialist at the University and Jepson Herbaria at the University of California – Berkeley, where she earned both her bachelor's and doctoral degrees in integrative biology. She is a geneticist and botanical taxonomist whose focuses include the development of DNA-technology-based botanical authentication methods, as well as the study of and conservation strategies for sandalwoods (*Santalum* spp., Santalaceae). Dr. Reynaud has served as a reviewer for academic journals such as *Molecular Phylogenetics and Evolution*, *Journal of Biogeography*, and the *Botanical Journal of the Linnaean Society*.

Navindra Seeram, PhD, is an assistant professor of pharmacognosy at the University of Rhode Island's College of Pharmacy, where he runs the Bioactive Botanical Research Laboratory. He previously was the assistant director of the David Geffen School of Medicine's Center for Human Nutrition at the University of California – Los Angeles. Dr. Seeram — who received his doctoral degree in natural products chemistry from the University of the West Indies in Kingston, Jamaica — focuses his research on traditional medicines and botanical extracts, particularly examining how they might prevent or treat chronic illnesses. He has been the recipient of several awards and honors, including the American Chemical Society's 2009 Young Scientist Award. Dr. Seeram publishes in numerous scientific journals and helps organize conferences for the natural products community.

Alexander G. Schauss, PhD, is the senior research director at Natural and Medicinal Products Research and CEO at AIBMR Life Sciences in Puyallup, Washington. As lead scientist, Dr. Schauss has worked on projects in 44 countries for AIBMR to support research activities and deal with regulatory matters for over 500 companies or institutions. He earned his undergraduate, graduate, and doctoral degrees at the University of New Mexico at Albuquerque and California Coast University in Santa Ana, respectively. Dr. Schauss is a Fellow of the American College of Nutrition, and a member of the American Society of Nutrition, the Society for Experimental Biology in Medicine, and the Association for African Medicinal Plants Standards, among others. In 2005, he received the Linus Pauling Lecture Award for contributions to the medical sciences from the American College for the Advancement of Medicine. Dr. Schauss is the author or co-author of over 200 publications, and the author or co-author of 23 books in the fields of nutrition and botanical medicine.

Paul E. Stamets is the founder, owner, and managing director of Fungi Perfecti, LLC, founder and managing director of Agarikon Press and The Life Box Company, as well as the owner and managing director of Mycopesticide, LLC. Widely acknowledged as North America's premier advocate for medicinal mushrooms and fungi for bioremediation, Stamets has been a mycologist for more than 30 years, during which he discovered four new species of mushrooms and pioneered techniques in the field of edible and medicinal mushroom cultivation. A graduate of Kenyon College and The Evergreen State College, he is a member of the GMP/GAP Board on Standards for Production of Medicinal Plants/Medicinal Mushroom Production for the US Pharmacopeia, on the editorial boards for *The International Journal on Medicinal Mushrooms* and *Mushroom, the Journal*, and an advisor to the Program for Integrative Medicine at the University of Arizona Medical School. In 2008, Stamets received National Geographic Adventure Magazine's Green-Novator and Argosy Foundation's E-chievement awards. Stamets is the author of six books on mushroom cultivation and has presented a TED talk on the vast health and environmental benefits of mushrooms, titled "Six Ways Mushrooms Can Save the World." HG

ABC NEWS

More Than 100 Groups Support ABC-AHP-NCNPR Botanical Adulterants Program

The American Botanical Council-American Herbal Pharmacopoeia-National Center for Natural Products Research (ABC-AHP-NCNPR) Botanical Adulterants Program announces that it has reached the milestone of having more than 100 underwriters and endorsers. They include some of the biggest names in the botanical and dietary supplement community, including botanical dietary ingredient suppliers, supplement manufacturers, trade and professional associations, colleges and universities, analytical laboratories, contract research organizations, media companies, and law firms.

Leading nonprofit organizations ABC, AHP, and NCNPR initiated this ongoing program in 2011 to educate members of the herbal and dietary supplement industry and numerous other stakeholders in the herb, dietary supplement, and natural medicine arenas about ingredient and product authenticity and adulteration.

"We are deeply gratified by the huge outpouring of support that we have received on this vitally needed educational program," said Mark Blumenthal, founder and executive director of ABC, and Program manager. "Wherever we have gone to solicit financial, technical, and other types of support, we have almost always received a positive response. This reflects the high level of concern that many responsible elements in the herb and natural health community — including, but not limited to, the herb and dietary supplement industry — have about the quality and reliability of herbal supplements, teas, etc. Even though it's apparent that there are many authentic, high-quality, reliable ingredients and products, the fact remains that there are identity and quality problems that have persisted far too long, and now many of us are circling the wagons to reduce and hopefully eliminate some of the errors and fraud that exist in this field."

"We are deeply gratified by the huge outpouring of support that we have received on this vitally needed educational program."

The ABC-AHP-NCNPR Botanical Adulterants Program focuses on both accidental adulteration that may occur due to inadequate quality control procedures, as well as intentional adulteration of plant-based ingredients for financial gain. In an industry that saw sales rise 4.5% in 2011 to an estimated figure of nearly $5.3 billion in herbal dietary supplement product retail sales in the United States alone, documented cases of adulteration of raw materials, *i.e.*, problems related to ingredient authenticity and quality, is a matter of growing concern.

Title 21 of the US Code of Federal Regulations defines adulteration as the "[a]ddition of an impure, cheap, or unnecessary ingredient to cheat, cheapen, or falsify an ingredient or preparation." The Code also deems a product adulterated "if any substance has been added thereto or mixed or packed therewith so as to increase its bulk or weight, or reduce its quality or strength, or make it appear better or of greater value than it is."

The primary intention of the ABC-AHP-NCNPR Botanical Adulterants Program is to help protect consumers and responsible members of the herb and dietary supplement industry, as well as other manufacturers, from purchasing adulterated raw materials. This is done by the Program's publishing a series of detailed articles that serve as an authoritative source of information on botanical adulterants. These articles contain references to published official and unofficial analytical methods for company and/or third-party quality control laboratories to consider using to detect the presence (or absence) of known adulterants.

To date, four papers on the topic of botanical adulteration have been published in *HerbalGram.* The first of these, "A Brief History of Adulteration of Herbs, Spices, and Botanical Drugs," written by noted botanical expert Steven Foster, appeared in the winter 2011 issue (#92). The article provides a history of accidental and intentional adulteration of botanical ingredients spanning the past two millennia.

In the spring of 2012, *HerbalGram* featured another article by Foster, covering the adulteration of skullcap with American germander. The herb skullcap (*Scutellaria lateriflora,* Lamiaceae), has been used as a mild sedative for more than a century, but, in the early 1980s, it became erroneously implicated as a possible source of liver toxicity, likely due to adulteration with or substitution of American germander (*Teucrium canadense,* Lamiaceae).

The third feature in the series is "The Adulteration of Commercial 'Grapefruit Seed Extract' with Synthetic Antimicrobial and Disinfectant Compounds," written by John H. Cardellina II, PhD, and published in *HerbalGram* #94. A popular ingredient in natural products, grapefruit seed extract (GFSE; *Citrus* x *paradisi*, Rutaceae) has appeared in cosmetics and dermatological preparations as well as dietary supplements. The article reviews 10 analytical studies published in international journals demonstrating that samples of GFSE were adulterated with various synthetic chemicals, including the disinfectant triclosan. The article concludes that a significant amount of GFSE is adulterated, or at least was at the time the 10 analyses occurred over a 20-year period, and that GFSE's promoted antimicrobial activity may be due to the presence of these synthetic antimicrobial adulterants, rather than the extract itself.

The most recent article in the series, "The Adulteration of Commercial Bilberry Extracts," also written by Foster, was published in the winter 2012 issue of *HerbalGram.* Bilberry fruit (*Vaccinium myrtillus,* Ericaceae) is a popular food in Europe where it grows wild throughout Scandinavia and Eastern Europe. It is also a best-selling supplement ingredient in the US marketplace. In a probable example of economically motived adulteration, it seems that many bilberry extracts are adulterated with a "confusing morass" of ingredients, including black soybean hull extract, amaranth dye (also known as Red Dye No. 2), charcoal, and various other fruits.

With more than 100 underwriters and endorsers of the ABC-AHP-NCNPR Botanical Adulterants Program, Blumenthal says that this widespread support will continue to bring the global problem of adulteration to the attention of members of the herbal and dietary supplement community.

"We will continue to invite more companies, organizations, and others — both in the US and internationally — to join with us in this educational quest to increase knowledge about authenticity and adulteration problems," said Blumenthal. "Adulteration is an ancient and global problem. With increased education through an effective program, we believe we can significantly reduce, perhaps even eliminate, some of the problems in the market."

In addition to the series of articles, the Adulterants Program includes contributions and consultations from some of the leading independent third-party laboratories with experience in quality control and botanical identification issues. The editorial committee, which advises on all technical publications, includes expert scientists from various universities, government agencies, and third-party analytical laboratories with extensive knowledge of herbal quality control. The Program also is being supported by leading trade associations in the dietary supplement industry, including the Consumer Healthcare Products Association, the Council for Responsible Nutrition, the Natural Products Association, and the United Natural Products Alliance.

A complete list of ABC-AHP-NCNPR Botanical Adulterants Program supporters can be found at http://abc.herbalgram.org/site/PageServer?pagename=Adulterants. HG

—Sara O'Connor

ABC Presents Annual Botanical Excellence Awards

The American Botanical Council held the 8th Annual ABC Botanical Celebration and Awards Ceremony on March 7, 2013, in Anaheim, California. As in previous years, ABC's event was held in conjunction with the Natural Products Expo West trade show and Nutracon scientific conference.

The event, held at the Marriott Anaheim, was attended by approximately 300 ABC Sponsor Members, Corporate Members, members of the ABC Board of Trustees, Advisory Board, and Director's Circle (a group of supporters who assist ABC's executive director with fundraising and educational efforts), and other supporters of ABC's nonprofit educational mission from academia and the natural products community. The evening was filled with dynamic conversations, opportunities to renew old relationships and establish new ones, delectable food and drink, and, of course, the honored award recipients.

The awards program itself began with one of ABC Founder and Executive Director Mark Blumenthal's signature slide shows of entertaining cartoons, which brought smiles and laughter to the crowd. ABC Board of Trustees Chairman Steven Foster announced the ABC James A. Duke Excellence in Botanical Literature Award recipients, including Martin A. Lee's *Smoke Signals: A Social History of Marijuana* in the Consumer/Popular category, and Rainer Bussmann, PhD, and Bruce Ponman's *Medicinal Plants and the Legacy of Richard. E. Schultes* in the Reference/Technical category.

Blumenthal presented Horphag Research, producer of Pycnogenol®, with the ABC Varro E. Tyler Commercial Investment in Phytomedicinal Research Award. Previous ABC Norman R. Farnsworth Excellence in Botanical Research Award recipient Joseph M. Betz, PhD, presented the ABC Farnsworth award to Professor De-An Guo, PhD, who traveled from Shanghai especially to accept the award in person.

ABC also presented, for the first time, its newly created Mark Blumenthal Herbal Community Builder Award. The inaugural recipient was celebrated herbalist, educator, and author Rosemary Gladstar, who accepted the award via a delightful pre-recorded video. "I have been hesitant to institute an award named after myself, of course, but the ABC Board of Trustees insisted," said Blumenthal. "I finally acquiesced because I have long wanted to honor Rosemary, and others like her (*if* there are any like her!), whose vital contributions fall outside of the previously existing ABC award categories."

Mark Blumenthal, ABC's Founder and Executive Director, hosts the 2013 ABC Celebration in Anaheim, CA. Photo ©2013 ABC

Crowd of ABC supporters enjoying the presentations made at the 2013 ABC Celebration. Photo ©2013 ABC

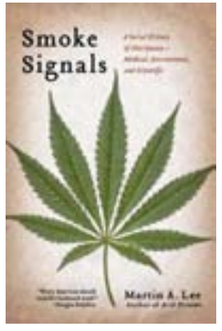
ABC James A. Duke Excellence in Botanical Literature

The ABC James A. Duke Excellence in Botanical Literature Award was created in 2006 in honor of noted economic botanist and author, James A. Duke, PhD. It is given annually to books that provide a significant contribution to literature in the fields of botany, taxonomy, ethnobotany, pharmacognosy, phytomedicine, herb safety, and other disciplines related to the vast field of medicinal plants. Among his prestigious career achievements in economic botany and ethnobotany at the United States Department of Agriculture (USDA), Dr. Duke has authored more than 30 reference and consumer books. He is also a co-founding member of ABC's Board of Trustees and currently serves as Director Emeritus.

In 2011, due to the diversity of quality books related to medicinal plants, ABC created two distinct categories for the James A. Duke Award. The recipient of the Consumer/Popular books category award was *Healing Spices: How to Use 50 Everyday and Exotic Spices to Boost Health and Beat Disease* by Bharat B. Aggarwal, PhD, and Debora Yost (Sterling Publishing, 2011). The same year, the American Herbal Pharmacopoeia's *Botanical Pharmacognosy: Microscopic Characterization of Botanical Medicines* (CRC Press) received the Reference/Technical books category award.

Smoke Signals: A Social History of Marijuana – Medical, Recreational, and Scientific

Martin A. Lee, who spent three-and-a-half years researching and writing the book, is an award-winning investigative journalist and co-author of *Acid Dreams: A Complete Social History of LSD – The CIA, The 60s, and Beyond* (Grove Press, 1985). The publication of *Smoke Signals* by Scribner, a division of Simon & Schuster, Inc., coincided with a robust public discussion of medicinal cannabis (*Cannabis* spp., Cannabaceae) during the 2012 election season. Currently, 18 states and the District of Columbia have legalized medicinal cannabis, and, last November, Colorado and Washington became the first states to decriminalize the possession of up to an ounce of cannabis for personal use by adults.



"When I began writing about cannabis, I had no idea about the impressive scientific data, mainly based on pre-clinical research, that powerfully validates the experience of many medical marijuana users," said Lee. "Public attitudes reflect conflicting claims about marijuana's potential benefits and risks. There has been a deliberate effort to create uncertainty about what the science says about cannabis. I would compare it to corporate-driven efforts to create scientific uncertainty with respect to climate change. The public discussion about marijuana continues to be haunted by the ghosts of *Reefer Madness*," he said, referring to the 1936 American propaganda film that heavily distorted the physical, psychological, and social effects of smoking cannabis.

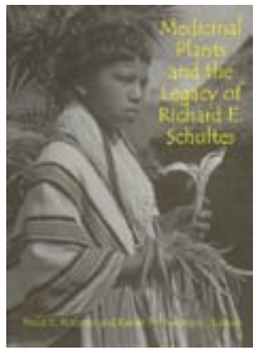
Foster explained the importance of public education and debate in a time when cannabis is still viewed by many as taboo. "We don't get to the next stage of understanding the phytochemistry, pharmacology, and medical potential, unless we go through a period of social revolt against the way things are and have been for far too long," he said. "And we don't get there as a society unless we do understand the social history. That is the only way that we as a society are going to move the science forward in a rational way."

"My exciting, sometimes dangerous, and always interesting career has seen me in the coca fields of Latin America, poppy fields in Laos, and *ganja* fields in Jamaica," said Dr. Duke, who worked for several years on a USDA collaboration with the Drug Enforcement Agency's anti-narcotic program, referring to frequently controversial and often-abused medicinal plants coca (*Erythroxylum coca*, Erythroxylaceae), poppy (*Papaver somniferum*, Papaveraceae), and cannabis. "Their programs targeted cannabis, the coca bush, and the opium poppy, each with long histories of major medicinal activities. [*Smoke Signals*] is historically important, but my greater interest is in the medicinal bullets that Lee presents."

The meticulously researched book aims to help educate readers to understand the long, often-contentious history of cannabis, including its use as medicine. According to the publisher's website, *Smoke Signals* "draws attention to underreported scientific breakthroughs that are reshaping the therapeutic landscape." Medicinal cannabis has been studied as a potential treatment for a wide variety of health conditions including chronic pain, cancer and chemotherapy side effects, and heart disease, among many others.

"I'm very pleased that the American Botanical Council recognizes the importance of clear, incisive reporting about cannabis," said Lee. "The plant deserves it."

Medicinal Plants and the Legacy of Richard E. Schultes



This book, a collection of essays published by the Missouri Botanical Garden, is based on the proceedings of the 2011 symposium held in honor of the great ethnobotanist and Harvard University Professor Richard E. Schultes, PhD (1915-2001), on the 10th anniversary of his death.

"If anybody could be named as the father of ethnobotany, it would be Richard E. Schultes," said co-editor Dr. Bussmann. "No researcher has ever done more field research, more to promote the discipline, and has encouraged more students to become ethnobotanists, with almost every senior scientist in the field acknowledging some connection to Schultes."

The book chronicles the influence of Dr. Schultes on former students and colleagues and sheds light on his illustrious career and the lasting effects of the pioneering ethnobotanist. "I am increasingly of the belief that Richard Evans Schultes' impact has yet to be fully realized in terms of his historical importance," said ABC Board of Trustees President Steven Foster. "Roughly half of the chapter authors of the book were his students. Schultes' careful, conservative, high-quality scholarship quietly affected the social and political history of the last half of the twentieth century."

According to Dr. Bussmann, Dr. Schultes published roughly two dozen books and 500 papers, collected over 30,000 plant samples, and conducted continuous fieldwork in the Amazon for more than 14 years. "[He] created what can only be called the golden age of Economic Botany," he said.

"The symposium volume, like Schultes himself, is an ethnobotanical treasure," said Dr. Duke. "My thanks and congratulations to the editors and contributors for a notable symposium we can treasure forever."

"There is no doubt among those in the fascinating field of ethnobotany that Professor Schultes was the greatest ethnobotanist of our time, or possibly of any era," said ABC's Blumenthal. "His students were profoundly inspired by his teachings, and many have embraced ethnobotany and related fields as their primary passion and inspiration for their careers."

Many of Schultes' former students are part of ABC, either as members of the ABC Advisory Board or friends of the herbal community. These include, but are not limited to, the following scholars, authors, educators, and conservation botanists, among numerous others: Michael J. Balick, PhD, of the New York Botanical Garden; Wade Davis, PhD, explorer-in-residence at the National Geographic Society and best-selling author; Djaja D. Soejarto, PhD, at the College of Pharmacy at the University of Illinois - Chicago; Steven King, PhD, of Napo Pharmaceuticals; Mark Plotkin, PhD, director of the Amazon Conservation Team; Paul Alan Cox, PhD, executive director of the Institute for Ethnomedicine; Robert Bye, PhD, director emeritus of the Botanical Garden of the Institute of Biology of the National Autonomous University of Mexico; and the iconic integrative medicine pioneer and best-selling author Andrew Weil, MD.

Dr. Bussmann and Mr. Ponman were grateful to be chosen for the Excellence in Botanical Literature award, praising its namesake. "James Duke is one of the most respected colleagues in our field, and has for decades been the leader of the systematization and publication of ethnobotanical information and the phytochemical data associated with it," said Dr. Bussmann. "He is also one of the most prolific and widely read authors in the field. To receive the James Duke Award is an exceptional honor to us both as editors and the Missouri Botanical Garden."

Varro E. Tyler Commercial Investment in Phytomedicinal Research Award

The recipient of ABC's 2012 Varro E. Tyler Commercial Investment in Phytomedicinal Research Award, Switzerland-based Horphag Research, is the producer of Pycnogenol® French maritime pine bark (*Pinus pinaster,* Pinaceae) extract, which is used in hundreds of brands and formulas of dietary supplements, as well as in cosmetics, functional foods, and beverages.

"Horphag Research and its entire team are, of course, very honored to receive this prestigious award," said Victor Ferrari, CEO of Horphag Research. "It is an important recognition for the scientific work that has been established over so many years on one single and unique product — Pycnogenol."

HORPHAG

Horphag Research was founded in Berlin in 1925 as HormopharmaAG by Charles Haimoff. In the 1960s, Haimoff's vision of "healthy aging" led to the development of the antioxidant French maritime pine bark extract, Pycnogenol. Research on the product began in 1965, and, just two years later, the first preparations were being sold in Europe. By 1987, Horphag was awarded its first US patent, and in 2003 Pycnogenol was self-affirmed to be GRAS (Generally Recognized as Safe) for use in food products. Sales of Pycnogenol products to consumers now exceed $500 million annually and are sold in more than 80 countries around the world.

"For 40 years, Horphag has invested in extensive research to ensure the safety and efficacy of Pycnogenol as a premium ingredient," said Frank Schönlau, PhD, scientific director for Horphag Research. "For more than a decade, I have personally overseen much of the research as we have built upon that commitment. I am extremely proud to see the team recognized for its dedication to making Pycnogenol one of the most well-researched natural health supplements available today."

"ABC congratulates Horphag Research for this most well-deserved and probably overdue honor," said Blumenthal. "Horphag Research is the epitome of a research-based natural products company, investing millions of dollars in scores of clinical research trials on its key product, Pycnogenol.

"Professor Varro Tyler was one of my key mentors for about 20 years. He repeatedly emphasized his desire to see herb companies invest in scientific and clinical research on their herb and phytomedicinal products. I have no doubt that if he were alive today, he would fully endorse ABC's choosing Horphag this year to receive his eponymous award," continued Blumenthal.

The late Professor Tyler — who has been described as one of the most respected men in late 20th century herbal medicine and pharmacognosy (the study of medicines of natural origin, usually from plants) — was an early trustee of ABC, dean of the College of Pharmacy and Pharmaceutical Sciences at Purdue University, and vice-president of academic affairs at Purdue. He was the senior author of six editions of the leading textbook in the field, formerly used in every college of pharmacy in the United States.

Professor Tyler urged his students and colleagues "not only to seek the truth but, after finding it, to discard any preconceived ideas which it may reveal as untrue." He encouraged scientific and product integrity and envisioned a rational herbal healthcare sector that valued the proper evaluation of products' quality, safety, and efficacy.

"Receiving the American Botanical Council's Tyler Award provides not only credibility to our scientific work, but also a tremendous motivation to our team to continue providing scientific evidence on a multitude of health benefits of Pycnogenol," said Ferrari. "We are not only blessed with one of the most versatile and well-documented products in this industry, but also with the most professional and dedicated team."

According to Horphag, the extensive study of Pycnogenol has resulted in more than 100 published clinical studies and 300 scientific publications in total (chemistry, *in vitro* laboratory studies, animal pharmacology and toxicology studies, review articles, etc). Horphag Research's bibliography includes studies on a diverse group of topics, including antioxidant properties, cardiovascular health, skin care, joint health, sports nutrition, and more. Recently published clinical studies show the abilities of Pycnogenol to reduce perimenopausal symptoms, improve skin hydration and elasticity, reduce asthma symptoms, and improve endothelial function.

This proliferation of research and the popularity of Pycnogenol products are likely what caught the eye of celebrated surgeon and TV host Mehmet Oz, MD, who spent a segment of his "Dr. Oz" show in December 2012 discussing the benefits of Pycnogenol for younger-looking skin. The effects extolled by Oz are perfectly in line with the company's motto of helping people "look, feel, and live better."

Previous recipients of ABC's Tyler Award include Schwabe Pharmaceuticals (2008), Indena SpA (2009), Bionorica AG (2010), New Chapter Inc. (2011), and Bioforce (2012).

Norman R. Farnsworth Excellence in Botanical Research Award

Professor De-An Guo, PhD

Over the course of his career, ABC Farnsworth Award recipient Professor De-An Guo's research has centered on Traditional Chinese Medicine (TCM) quality control, biochemistry, and metabolism; his phytochemical investigations of traditional Chinese herbal medicines have resulted in the identification of 100 new chemical entities. In addition to his professorship, Dr. Guo serves as director of the State Engineering Laboratory for TCM Standardization Technology and as director of the Shanghai Research Center for TCM Modernization at the Shanghai Institute of Materia Medica of the Chinese Academy of Sciences. He earned his doctorate in pharmacognosy from Beijing Medical University's School of Pharmaceutical Sciences in 1990, and conducted his postdoctoral studies in the department of chemistry and biochemistry at Texas Tech University in Lubbock, Texas.

Among his many accomplishments, including more than 430 published scientific papers to date, Dr. Guo acted as the vice-editor-in-chief of the 2005 edition of the *Pharmacopoeia of the People's Republic of China* and editor-in-chief of the 2010 edition. At present, he sits on the editorial boards of several highly respected international scientific journals, including *Planta Medica* and *Phytomedicine*. Dr. Guo is an expert committee member of the United States

Pharmacopeia and a member of the ABC Advisory Board.

"Professor Guo is not only an established scientist, he has provided leadership in the modernization of TCM," said past recipient of ABC's Farnsworth Award, Professor Ikhlas Khan, PhD, a research professor of pharmacognosy and associate director of the National Center for Natural Products Research at the University of Mississippi. "He is a deserving recipient and I am proud to call him my friend."

The Excellence in Botanical Research Award's namesake is ABC's co-founding Board of Trustees member, the late Professor Norman R. Farnsworth, PhD, a research professor of pharmacognosy and senior university scholar in the College of Pharmacy at the University of Illinois – Chicago. When Professor Farnsworth died in 2011 at the age of 81, the medicinal plant community lost one of its greatest champions. ABC will continue to present this award each year to a person or institution that has made significant contributions to ethnobotanical and/or pharmacognostic research.

"We are most pleased to be able to recognize and honor Professor Guo for his outstanding achievements in the chemistry and pharmacology of many traditional Chinese medicinal plants," said Blumenthal. "He is clearly one of the leading figures in scientific medicinal plant research in China, a country with a vast spectrum of traditionally used medicinal plants that are undergoing modern scientific research and validation."

"I am very pleased and honored to receive the high distinction of ABC's Norman R. Farnsworth Excellence in Botanical Research Award. I would like to thank ABC and the nominating committee who selected me for this award," said Dr. Guo. "This reflects the world-wide coverage of ABC's Farnsworth Award," he continued.

Previous recipients of ABC's Norman R. Farnsworth Excellence in Botanical Research Award include Dr. Betz, of the Office of Dietary Supplements at the US National Institutes of Health (2006); Professor Edzard Ernst, MD, PhD, formerly of the Peninsula Medical School at the University of Exeter in the United Kingdom (2007); Professor Hildebert Wagner, PhD, of the Institute for Pharmaceutical Biology in Munich, Germany (2008); Dr. Khan (2009); Professor Rudolf Bauer, PhD, head of the Institute of Pharmaceutical Sciences at the Karl-Franzens University of Graz in Austria (2010); Professor A. Douglas Kinghorn, PhD, chair of the department of medicinal chemistry and pharmacognosy in the College of Pharmacy at Ohio State University (2011); and Professor Djaja D. Soejarto, PhD, of the College of Pharmacy at the University of Illinois – Chicago (2012).

Mark Blumenthal Herbal Community Builder Award

The first Mark Blumenthal Herbal Community Builder Award recipient, Rosemary Gladstar, is a renowned herbalist, teacher, and author known to many as the Godmother of American Herbalism. Among her many accomplishments and efforts that have helped grow a rich herbal community in the United States, Gladstar founded several schools of herbal education, founded and organizes annual herbal conferences, leads international herb-focused journeys, and has authored or co-authored about a dozen books on topics ranging from herbal medicine recipes to medicinal plant conservation.

"I know of no other herbalist who has done more to create a sense of relationship, community, and identity among herbalists and others with a strong interest in herbs and herbal healing than Rosemary," said Blumenthal. "Her energy, enthusiasm, passion, creativity, love, and generous spirit are bountiful and contagious. There is no one like her."

Gladstar, the daughter of Armenian immigrants, first learned plant medicine during informal garden walks with her grandmother, Mary Abelian Egitkanoff. She was instantly interested in the plant world, which was apparent in the middle school projects she chose to do on medicinal herbs. In the early 1970s, Gladstar opened her own herb shop, Rosemary's Garden, in Sonoma County, California. Then, in 1974, she co-founded the tea company Traditional Medicinals with Drake Sadler and created many of the teas' original formulations, including the popular Smooth Move®, Throat Coat®, and Mother's Milk®. In 1978, she founded the California School of Herbal Studies (CSHS), which is still in operation today as the country's oldest herbal school. In the following years, she founded the Breitenbush Herbal Conference, the International Herb Symposium, and the New England Women's Herbal Conference — the latter two of which she still directs.

"In those early days," said Gladstar, "when herbalism and herbalists were first peeking up from 'underground' — where they had rested quite contentedly, it seems to me, for a number of decades — there really wasn't very much going on herbally at all. We were rather isolated; there weren't newsletters, gatherings, or schools that I know of in the US that served to bring us together. [So,] these early gatherings were revolutionary, really, and had a lot to do, I think, with nourishing and creating an herbal community. When I look at plant communities, they thrive together. The greater the diversity in the garden (or meadow or woodland), the better the health of the community. And it's certainly true of herbalists, as well."

Rosemary Gladstar

In the 1980s, Gladstar created Sage Mountain Herbal Retreat Center, a 500-acre botanical sanctuary in Vermont where she currently lives and hosts educational events and programs. Additionally, she runs her commended herbal home-study course, "The Science & Art of Herbology," and has been leading the internationally focused Plant Lovers Journeys since 1986. Gladstar's several books on herbs — including *Herbal Healing for Women*, *Rosemary Gladstar's Family Herbal*, and the 2012 *Rosemary Gladstar's Medicinal Herbs: A Beginner's Guide* — regularly sell well and receive glowing reviews from her herbal peers and loyal readers. The United Plant Savers, which Gladstar founded in 1994, remains the project that she is most passionate about due to its focus on preserving and conserving native North American medicinal plants and their habitats from unsustainable wild-collection. She continues to serve on the group's Board of Directors as founding president.

"For Rosemary, the linking of herbs to humans is only a mechanism for people to bring awareness to Mother Earth from whom we all originate," said Steven Foster. "Rosemary laid the foundation for the rise of traditional herbalism, which has blossomed into touching the hearts of and teaching tens of thousands of people. Small gatherings of a couple dozen folks of like mind grew into international conferences, symposia, classes, and retreats that were key to the rise of two generations of practicing herbalists in the modern herbal renaissance."

"Rosemary Gladstar introduced herbalists to each other, and to the world," said fellow herbalist, the late Cascade Anderson Geller. "She gave herbalism a face, approachable and lovable. She gave a big leg up to herbalists of current renown, helping them to achieve success and grow their reputations. [She also] is a brilliant business woman. All of her businesses, even when she has moved on, continue to flourish in some form. To achieve such success, and to be so well loved by colleagues and students alike, is remarkable. Her trustworthiness shines because it is legitimate emanating from an open heart and mind with roots entwined deep in Mother Earth. By walking her talk, Rosemary's achieved incredible energy that she has generously shared."

Ever humble and modest, Gladstar gives much credit to her herbal peers. "We help each other grow," she said, "either by pushing, pulling, encouraging, tugging, or just pure nourishing love. At this point in time, the herbal community is really comprised of many communities, all interlinking through our love of plants. But as extraordinary as the plants that bring us together and unite us as an herbal community, are the people who love plants. They are an amazing group of diverse, bright, eccentric, talented, and amazing individuals. I count my lucky stars to be amongst them…. Again, I am humbled and honored by this award."

ABC members are welcome to nominate persons, books, and companies for the respective awards for consideration by the ABC Board of Trustees. Nominations can be made by emailing abc@herbalgram.org. HG

Review Supports Chaste Tree Berry Extracts for Female Reproductive Conditions

Reviewed: van Die MD, Burger HG, Teede HJ, Bone KM. *Vitex agnus-castus* extracts for female reproductive disorders: a systematic review of clinical trials. *Planta Med*. November 2012; [epub ahead of print]. doi: 10.1055/s-0032-1327831.

Chaste tree (*Vitex agnus-castus*, Lamiaceae) berry (VAC) is used for a range of female reproductive conditions, including premenstrual syndrome (PMS) and associated cyclic mastalgia (breast pain), premenstrual dysphoric disorder (PMDD; severe PMS), lactation difficulties, low fertility, and menopause-related complaints. These authors conducted a systematic review to evaluate the evidence of the efficacy and safety of VAC extracts from randomized, controlled trials (RCTs) investigating the effects of various VAC preparations on women's health.

The authors searched the following electronic databases from earliest publication to 2012: Medline, PubMed, EMBASE, The Cochrane Library, CINAHL, Ovid, Google Scholar, and Web of Science. They searched for RCTs, including crossover trials, of VAC versus placebo or a comparator treatment, with no language restrictions. They extracted details of trial design, duration and setting, condition under investigation, sample size, participants, outcome measures, adverse events, and results. The Jadad scale and the Cochrane risk of bias were used to measure the trials' methodological quality.

Chase Tree Berry *Vitex agnus-castus*.
Photo ©2013 Steven Foster

Thirteen trials were identified; twelve trials met the inclusion criteria for this review. Three of the trials continued for two menstrual cycles or months, one continued for six cycles, and eight lasted for three cycles or months; one of them, after a two-month washout, re-administered the same extract treatment on only the last seven days of the luteal phase for another three-month period. Of the 12 RCTs, eight investigated the effects of VAC extracts in women suffering from PMS,[1-8] two examined VAC in PMDD,[9,10] and the other two investigated latent hyperprolactinemia (LHP) with or without mastalgia.[11,12]

Six of the PMS studies were placebo-controlled; one compared the effects of VAC with those of pyridoxine (vitamin B_6); and another one compared VAC with magnesium. Both RCTs on PMDD compared VAC extracts with fluoxetine (Prozac®, Eli Lilly & Co.). Of the two trials investigating LHP, one was placebo-controlled and the other compared VAC with bromocriptine (a conventional drug used to treat LHP, among other conditions).

Five studies reported sample-size calculation estimates ranging from 55 to 120 subjects per arm. Six studies included data from more than 100 subjects (ranging from 110 to 217).

Eight different outcome measures were used in the RCTs investigating PMS and PMDD. Symptoms were measured by the premenstrual tension syndrome (PMTS) self-rating scale and the premenstrual syndrome diary (PMSD), as well as visual analogue scales and the Hamilton Rating Scale for Depression.

The authors reported that for PMS, VAC extract was superior to placebo in five of the six studies (with a total of 1067 subjects), leading most of the investigators of those studies to conclude that VAC was effective and well-tolerated for the relief of mild-to-moderate PMS symptoms. It also was superior to pyridoxine in one study (105 subjects).[8] In the study comparing the use of VAC to magnesium (82 subjects), PMS symptoms were more improved in the VAC group than in the magnesium group for all variables (back pain, menstrual pain, breast fullness, headache, asthenia, irritability, and sleep disturbances).[7]

Regarding PMDD, one study with 38 subjects reported clinical improvement in both the VAC and fluoxetine groups, with 57.9% of subjects responding to VAC, and 68.4% responding to fluoxetine.[10] The authors proposed that "fluoxetine may be more effective for psychological symptoms while VAC may be more effective for physical symptoms." In the other PMDD study, with 57 subjects, fluoxetine outperformed VAC on all endpoints — depressed mood, work interests, psychic anxiety, and general somatic symptoms; simultaneously, the VAC group significantly improved on all endpoints.

Of the LHP studies, one trial reported VAC to be superior to placebo in treating luteal phase defects due to LHP, as evidenced by its role in reducing thyrotropin-releasing hormone-stimulated prolactin secretion, normalizing a shortened luteal phase, and increasing mid-luteal progesterone and 17β-estradiol levels. In another study, VAC was comparable to bromocriptine in reducing serum prolactin levels and ameliorating cyclic mastalgia.[11]

Because of the "range of conditions under investigation, outcome measures, and expression of results," the authors could perform a meta-analysis on only two of the PMS studies. Combining the results of the multicenter study reporting total PMS symptoms on the PMSD and PMTS scales[3] (including 217 subjects) with the outcome reported on the Penn Daily Symptom Report[4] (with 116 subjects), VAC showed a greater benefit than placebo.

Adverse events associated with VAC were mild, generally infrequent, and less severe than those reported with fluoxetine or bromocriptine.

The methodological quality of the included studies varied, but was generally moderate to high. Even with the methodological limitations, the RCTs to date appear to support the efficacy and tolerability of VAC extracts in the treatment of PMS, PMDD, and LHP. "However, lack of transparency in the reporting of some studies limits assessment of trial design and, in some cases, results. Future research into *Vitex* extracts for these conditions would benefit from use of tightly defined patient populations and common endpoints," concluded the authors.

Agnucaston® (Bionorica; Neumarkt, Germany), Ze 440 (Zeller AG; Romanshorn, Switzerland), Agnolyt® (Madaus GmbH; Cologne, Germany), and Monoselect Agnus® (PharmExtracta; Pontenure, Italy) were among the commercial products used in the trials in which products were specified.

—Shari Henson

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Clinical Trial Shows Aged Garlic Extract™ Supplementation Reduces Blood Pressure

Reviewed: Ried K, Frank OR, Stocks NP. Aged Garlic Extract reduces blood pressure in hypertensives: a dose-response trial. *Eur J Clin Nutr.* 2013;67(1):64-70.

Standard hypertension treatment with medication that lowers high blood pressure is ineffective in some people. Studies show that aged garlic (*Allium sativum*, Liliaceae) supplements can lower blood pressure. Aged Garlic Extract™ contains S-allylcysteine, a bioavailable and stable water-soluble organosulfur compound. The purpose of this randomized, double-blind, placebo-controlled study was to evaluate the effect and tolerability of different doses of Aged Garlic Extract as an adjunct treatment for patients with uncontrolled hypertension.

Seventy-nine patients (mean age: 70 years) with uncontrolled hypertension (systolic blood pressure [SBP] ≥ 140 mmHg in the past six months) from two general practices in Adelaide, South Australia, participated in this study conducted from August 2011 to March 2012. Included patients had taken prescription antihypertensive medication for two months or longer, and their general practitioners did not intend to change the medication plan during the trial. Excluded patients had an unstable or serious illness or already were taking garlic supplements. Patients received one, two, or four capsules per day of Kyolic® High Potency Everyday Formula 112 (Wakunaga/Wagner; Sydney, Australia; Kyolic® Aged Garlic Extract is produced in Japan by Wakunaga), containing 240, 480, or 960 mg of Aged Garlic Extract (AGE) and 0.6, 1.2, or 2.4 mg Sallylcysteine, respectively, or placebo, for 12 weeks. Sachets with a drop of liquid Kyolic were added to the placebo containers as a method of blinding. Patients were instructed to take their usual prescription medication.

The primary outcome measures were SBP and diastolic blood pressure (DBP) at four, eight, and 12 weeks compared to baseline. The baseline characteristics were similar between groups. Patients took an average of two different types of antihypertensive medications. At 12 weeks, the two-capsule (480 mg) group showed a significant reduction in SBP compared to placebo (P=0.03). There was no change in DBP. The authors conducted an additional analysis that excluded five patients from the data set who had blood pressure medication changes or poor compliance. In this additional analysis, the two-capsule group had a significant reduction in SBP compared to placebo at both eight and 12 weeks (P=0.006). There was no significant improvement in the one-capsule or four-capsule group compared with placebo at any point in either analysis. Across all groups, blood pressure changed from -40 to +5 mmHg. SBP did not change by > 5 mmHg in one-third of the participants. This finding was unassociated with sex, age, body mass index, smoking status, or number of blood pressure medications. One-third of the patients correctly guessed their treatment allocation.

Participants in the garlic groups reported minor complaints in the first week of the trial, including constipation, bloating, flatulence, reflux, garlic taste, and difficulty swallowing the capsules (23 percent). The difference in reported minor adverse side effects between those taking garlic capsules and those taking the placebo was not statistically significant.

The authors concluded that AGE was superior to placebo in lowering SBP in patients with uncontrolled hypertension. The two-capsule dose was effective and well tolerated. The authors wrote that the effect was clinically significant because the 10 percent improvement in SBP is known to be associated with a decreased risk in cardiovascular disease. The authors stated that the study was not powered to detect a difference in DBP because the patients were selected based on their SBP. Currently, it is thought that DBP is an important predictor of cardiovascular disease and may be a more important determinant than SBP. The authors should re-examine the two-capsule dose in a patient sample powered to determine whether AGE has an effect on DBP. HG

—Heather S. Oliff, PhD

Garlic *Allium sativum*. Photo ©2013 Steven Foster

Artichoke Leaf Extract Improves HDL Cholesterol Levels in Patients with Hypercholesterolemia

Reviewed: Rondanelli M, Giacosa A, Opizzi A, *et al.* Beneficial effects of artichoke leaf extract supplementation on increasing HDL-cholesterol in subjects with primary mild hypercholesterolaemia: a double-blind, randomized, placebo-controlled trial. *Int J Food Sci Nutr.* February 2013;64(1):7-15.

Cardiovascular disease (CVD) is a prevalent worldwide threat to health. Nutritional modifications, such as low-fat diets, typically are used to prevent or lessen CVD risk. However, diets targeting the reduction of harmful low-density lipoprotein (LDL) cholesterol also may reduce the concentration of beneficial high-density lipoprotein (HDL) cholesterol. Thus, interventions that reduce LDL while promoting higher concentrations of HDL are necessary for the alleviation of CVD. Artichoke (*Cynara scolymus*, Asteraceae) leaf extract (ALE) has been shown to lower cholesterol in previous studies. This randomized, double-blind, placebo-controlled study investigated the effects of eight weeks of ALE supplementation on HDL, LDL, and total cholesterol concentrations in subjects with hypercholesterolemia.

The 92 study participants were "mildly" hypercholesterolemic (5.4-7.0 mmol/l), 18 to 60 years of age, had a body mass index (BMI) range from 19 to 30 kg/m^2, and were recruited from the University of Pavia in Pavia, Italy. They did not have CVD or chronic diseases and were not on medicine that targeted cholesterol concentrations. The study excluded those who smoked tobacco, consumed excessive amounts of alcohol or weight-loss drugs, or were pregnant, lactating, or in menopause. Subjects were instructed to maintain their normal level of exercise and a three-day baseline dietary assessment was taken. This information was used to standardize subjects' diets to total caloric levels similar to American Heart Association recommendations; diet also was evaluated at the end of the study.

Blood pressure, body weight, and BMI, as well as skinfold thickness and abdominal diameter, were measured both at the beginning and at the end of the study. Treatments consisted of 250 mg tablets of either ALE or "a matching placebo" (excipients without ALE) administered before lunch and dinner (500 mg total daily dosage) for eight weeks. ALE was standardized to contain more than 20% caffeoylquinic acids, 5% flavonoids, and 5% cynaropicrin. [Note: No description of the placebo is given.] Both the ALE and placebo tablets were supplied by Indena SpA; Milan, Italy. Leftover tablets were used to gauge compliance.

Fasting LDL, HDL, total cholesterol, and glucose concentrations were measured from blood samples taken at baseline and the study endpoint. Fasting HDL cholesterol also was assessed eight weeks after the study's conclusion. Tolerability of the treatments was estimated by blood pressure and blood chemistry at baseline and at the end of the study. Any adverse side effects were inquired about by investigators and reported by subjects.

Of the subjects enrolled, there were no dropouts reported and all participants — 46 in each group — completed the study. Blood pressure measurements of both groups were within a normal range at baseline and endpoint, and BMI did not significantly change in either group during the study. Beneficial HDL cholesterol levels, the primary endpoint, significantly increased in the ALE group (P<0.001), but remained unchanged in the placebo group. No significant changes were observed in blood glucose concentrations in either group. Total cholesterol was significantly lower in both the supplemented (P<0.001) and control (P<0.010) groups; the change in this parameter in the supplemented group was significantly greater than in the control group (P=0.012).

In addition, the total cholesterol-to-HDL cholesterol ratio at the end of the study was significantly lowered in the supplemented group as compared to baseline (P<0.001); no change was observed in the placebo group. The LDL cholesterol concentrations also were significantly lowered in both the supplemented and placebo groups (P<0.001 and P<0.05, respectively). In the supplemented group, the LDL cholesterol-to-HDL cholesterol ratio significantly decreased (P<0.001), but remained unchanged in the placebo group. Triglycerides were not significantly altered in either group. Compliance was rated as "excellent," and no adverse side effects were reported. In addition, blood chemistry was normal in all subjects both at baseline and endpoint of the study.

In conclusion, this study reports a significant increase in HDL cholesterol with a concurrent decrease in LDL cholesterol in patients with hypercholesterolemia after eight weeks of supplementation with ALE. The authors note that an inverse relationship exists between HDL cholesterol and CVD risk, with a three percent reduction in death risk or myocardial infarction for every one percent increase in HDL cholesterol. Therefore, the clinical applications of ALE for this purpose may be beneficial, but warrant further study.

Possible mechanisms for the observed bioactivity include the modulation of various enzymatic activities by ALE compounds. For example, previous studies have shown that the ALE compounds chlorogenic acid and luteolin possibly attenuate LDL cholesterol oxidation and related damage. Luteolin, in addition, inhibits coenzyme A reductase activity, which is a key enzyme in the liver cholesterol synthesis pathway. Finally, chlorogenic acid could favor the HDL cholesterol increase through the agonistic effect on paraxonase-1, which is involved in the protection of HDL cholesterol from oxidation.

One important avenue of future research into ALE is the investigation of gender-related effects, as certain parameters measured — HDL cholesterol, in particular — have shown differences when data is stratified by gender. This suggests potential variable responses to ALE supplementation. Furthermore, given the marked sensory properties of cynaropicrin (bitter) and cynarin (sweet aftertaste), more information on the nature of the placebo should have been included in the publication. HG

—Amy C. Keller, PhD

Prospective Study and Meta-Analysis of Chocolate and Reduction of Stroke Risk

Reviewed: Larsson SC, Virtamo J, Wolk A. Chocolate consumption and risk of stroke: a prospective cohort of men and meta-analysis. *Neurology.* 2012;79(12):1223-1229.

Much evidence has accumulated to show that cocoa (*Theobroma cacao*, Sterculiaceae) and chocolate may have benefits for cardiovascular health through antioxidant, antiplatelet, anti-inflammatory, and blood pressure-lowering effects. In this paper, effects on stroke have been examined in four studies, with two having statistically significant results. However, none of these studies examined exclusively male populations, and only one made its evaluation based on stroke type. The prospective study assessed the association between chocolate consumption and risk of stroke and stroke subtypes in a cohort of Swedish men. In addition, the authors conducted a meta-analysis of prospective studies involving chocolate and stroke risk.

The study used data from the 1997 Cohort of Swedish Men (aged 45 to 79 years). Questionnaires with 350 items on diet and lifestyle were gathered from 48,850 men who were a good representation of the general population with respect to age distribution, relative body weight, and education level, compared with representative data from the Official Statistics of Sweden. After excluding questionnaires that were not completely filled in, and patients who had died or had a history of cancer, cardiovascular disease, diabetes, or an implausible total energy intake, 37,103 men remained.

Cocoa *Theobroma cacao.* Photo ©2013 Steven Foster

Consumption of chocolate was assessed using a self-administered food-frequency questionnaire that included 96 foods and beverages. Consumption in grams was computed by multiplying the frequency of chocolate consumption by four age-specific portion sizes (43-54 years, 42 g; 55-63 years, 34 g; 64-71 years, 27 g; 72-77 years, 26 g), which were obtained from the authors' validation study in Swedish men. Approximately 90 percent of chocolate consumption during the time frame of the study was in the form of milk chocolate.

Incidence of stroke was identified via the Swedish Hospital Discharge Registry and was classified as cerebral infarction (ICD-10 [International Statistical Classification of Diseases and Related Health Problems 10th Revision] code I63), intracerebral hemorrhage (I61), subarachnoid hemorrhage (I60), and unspecified stroke (I64).

In 10.2 years of follow-up, 1,995 cases of first-time stroke were identified, including 1,511 cerebral infarctions, 321 hemorrhagic strokes (254 intracerebral hemorrhages and 67 subarachnoid hemorrhages), and 163 unspecified strokes.

Patients in the highest quartile of chocolate consumption (62.9 g/week) had a statistically significantly lower risk of total stroke by 17 percent (95% confidence interval [CI]: 1-30) after adjustment for age and stroke risk factors, including blood pressure. This association was similar across stroke types. There was an inverse relationship between chocolate consumption and risk of total stroke observed in men without hypertension (relative risk [RR]: 0.76; 95% CI: 0.62-0.93), but not in men with a history of hypertension (RR: 1.04; 95% CI: 0.77-1.41; P for interaction = 0.04). The age-standardized incidence rates of stroke were 85 per 100,000 person-years among men in the lowest quartile of chocolate consumption and 73 per 100,000 person-years among men in the highest quartile.

For the meta-analysis, the databases PubMed and EMBASE were searched up to January 13, 2012, with no restrictions imposed. Four prospective studies examining the association between chocolate consumption and stroke were identified, plus the current study, making a total of five. These studies included a total of 4,260 stroke cases over a range of eight to 16 years of follow-up. Highest and lowest consumption of chocolate were compared, and dose response also was analyzed.

The RR of stroke in the highest compared to the lowest quartiles of chocolate consumption was 0.81 (95% CI: 0.73-0.90), with no heterogeneity. Dose response could be assessed in four out of five of the studies; for a 50 g increment per week, the RR was 0.86 (95% CI: 0.76-0.97), with no heterogeneity among studies (P=0.21; I^2=34.1%).

The highest levels of chocolate consumption were associated with a decreased risk of stroke in men, and this was confirmed by the meta-analysis. The results can be extrapolated to men in general because of the wide representation of men present in the sample population. Though the exact mechanism of action for the stroke benefit has not been elucidated, it is likely due to the pleiotropic (producing multiple effects from one gene) cardiovascular benefits of chocolate, including the lowering of blood pressure. The strengths of the study are its large population and its nearly complete data regarding stroke incidence. Its limitations include a lack of differentiation between types of chocolate consumed, self-reporting of consumption, and evidence of small study effects in the meta-analysis. The authors caution that chocolate should be consumed in moderation because of its high fat and sugar content. HG

—Risa Schulman, PhD

Exploring the Peripatetic Maze of BLACK COHOSH ADULTERATION

A Review of the Nomenclature, Distribution, Chemistry, Market Status, Analytical Methods, and Safety Concerns of this Popular Herb

By Steven Foster

Black Cohosh *Actaea racemosa.* Photo ©2013 Steven Foster

Editor's note: This paper is part of the series published under the aegis of the ABC-AHP-NCNPR Botanical Adulterants Program, an educational program led by the American Botanical Council, the American Herbal Pharmacopoeia, and the National Center for Natural Products Research at the University of Mississippi. The Program is financially supported and/or endorsed by an international coalition of more than 100 herb and dietary supplement industry members, third-party analytical laboratories, professional and trade associations, nonprofit educational groups including accredited schools of natural medicine, industry media organizations, law firms, contract research organizations, and others.

Summary

Black cohosh root and rhizome and their preparations (*Actaea racemosa,* syn. *Cimicifuga racemosa*; Ranunculaceae) have been of considerable international market, scientific, and consumer interest for more than 60 years, particularly during the last 15 years in the United States. The increased market demand, nomenclatural confusion of related North American and Asian species, along with case reports of liver toxicity associated with products labeled as black cohosh, have led to both suspicion of and actual identification of economic adulteration of black cohosh commercial supplies. From the mid-1950s through the 1990s, a voluminous body of literature on black cohosh was published based on market experience and clinical use of black cohosh in Germany. Since the late-1990s, a significant body of new analytical chemical, pharmacognostic, pharmacological, and clinical scientific literature has been published relative to the identity, pharmacology, toxicology, and clinical applications of black cohosh. In 1999, the Department of Medicinal Chemistry and Pharmacognosy at the College of Pharmacy, University of Illinois - Chicago (UIC), under the direction of the late Norman R. Farnsworth, PhD, received funding from US National Institutes of Health (NIH) to establish the Center for Botanical Dietary Supplements Research. The emphasis of the Center's research focused on botanical dietary supplements that may improve women's health, especially in the areas of menopause, premenstrual syndrome and persistent urinary tract infections. Black cohosh became one of the Center's primary research subjects. That collective research serves as a model for overcoming challenges associated with research on botanicals (as dietary supplements), including acquiring and identifying plant species, isolating and identifying active constituents, elucidating mechanisms of action, and conducting phase I and phase II clinical studies.[1] Research interest in black cohosh also was emphasized by many other research groups, such as the group led by Edward J. Kennelly, PhD, at the Department of Biological Sciences, Lehman College and the Graduate Center, City University of New York, and others too numerous to name. In addition, various herb companies, commercial analytical laboratories, trade organizations, non-governmental organizations, and regulatory agencies have focused on contributing to the general knowledge and understanding of all aspects of black cohosh. This article reviews issues associated with the complexities of black cohosh adulteration, including botanical and nomenclatural considerations; trade and economic issues; various identification, analytical, and authentication challenges; alleged liver toxicity linked to adulterated products; and other data on economic adulteration of products labeled as black cohosh.

Black Cohosh *Actaea racemosa.* Photo ©2013 Steven Foster

Introduction

The root and rhizome of black cohosh are sold as whole, semi-whole, chopped, cut and sifted, dry powders, and liquid and dry extracts. They are widely available in dietary supplement and phytomedicinal formulations in the United States, Canada, Europe, Australia, and elsewhere. In modern phytotherapy, black cohosh preparations are used primarily for the treatment of menopausal symptoms, including hot flashes, heart palpitations, nervousness, irritability, sleep disturbances, tinnitus, vertigo, excessive perspiration, and depressive states associated with menopause, as well as for premenstrual discomfort and painful menstruation.[2] Historically, the botanical was specifically considered to have an affiliation with the nervous system and uterus, and was used for a host of nervous system disorders and as a uterine tonic and antispasmodic.[3]

Product forms with the most market experience and evaluation in clinical studies are Remifemin®, an oral formulation, standardized to triterpene glycosides, of an isopropanolic black cohosh extract,[4] and Menopret® (Klimadynon®), an ethanolic extract. Remifemin has been manufactured by Schaper & Brümmer GmbH & Co. KG (Salzgitter-Ringelheim, Germany) since 1956. Bionorica (Neumarkt, Germany) produces Menopret (Klimadynon).[5*]

Black cohosh raw materials and their extracts are widely known in the herb industry to be adulterated with related species of *Actaea* (syn. *Cimicifuga*) from China. The American Herbal Products Association (AHPA) provides information and links to analytical tools and methods to help identify adulteration of raw materials and ingredients through its Botanicals Authentication Program[6] and its Known Adulterants recommendations incorporated into AHPA's Guidance Policies.[7] According to AHPA, "The economic adulteration of black cohosh root and rhizome with other species is well established."[8]

A detailed microscopic identification of *A. racemosa* as well as closely related species are provided by the American Herbal Pharmacopoeia (AHP) in its recently published *Microscopic Characterizations of Botanical Medicines* (CRC Press, 2011).[3] AHP also published a comprehensive review of quality control and authentication specifications of black cohosh and its adulterants in its Black Cohosh Rhizome monograph (2002), which provides comprehensive guidance on known adulterants that includes the botanical, microscopic, and chemical analyses of black cohosh.[9]

Botanical, Taxonomic and Nomenclatural Considerations

The genus *Actaea* includes 28 species from the Northern Hemisphere.[10] Compton *et al*.[11-13] analyzed morphological and genetic data and supported the combination of the genus concepts of *Actaea, Cimicifuga*, and *Souliea* — essentially reverting to Linnaeus's 1753 concept of the genus *Actaea*. Previously, the major morphological basis for separating *Cimicifuga* from *Actaea* was fruit type. *Actaea* has a berry-like fruit and *Cimicifuga* has a dry follicle.

Black cohosh is an erect, smooth-stemmed perennial that grows from four-to-eight feet (75-250 cm) in height. The large, alternate, triternately compound leaves are borne on short, clasping petioles. The ovate, acute leaflets, two-to-three inches (3-8 cm) in length, are thin, smooth, and two-to-three-lobed with sharply double-serrate margins. The long, wand-like, white inflorescence, about one inch (2.5 cm) in diameter, are borne on a terminal branching spike-like raceme. The main feature of the flowers are the numerous showy stamens, consisting of slender filaments with white anthers. Four or five small, concave, greenish-white sepals are larger than the nearly inconspicuous, stamen-like petals. The solitary white pistil is smooth to somewhat pubescent and sessile (attached at the base without a stalk or petiole). The fruit is a dry, oval-ribbed follicle that splits along a ventricle suture with eight-to-10 triangular brown seeds in two rows. In the southern United States, it begins blooming in mid-to-late June. Toward the northern part of its range, blooming begins as late as early August.[14]

Voucher Specimens and Identification

Bennett and Balick (2008) emphasize the fact that in the field of medicinal plant research, unless a plant can be unambiguously identified, reproducibility — the fundamental underpinning of science — is uncertain. To aid reproducibility, a preserved herbarium specimen to which the correct scientific name has been applied should be deposited in a properly curated collection. Two common problems, they note, are the frequent misuse of binomials in medicinal plant publications, and the lack of author citations for binomials. In a PubMed search of 100 titles or abstracts on medicinal plants, they found that 20% contained errors in the botanical name, emphasizing that the misspelling of binomials is an inexcusable error.[15] For example, a PubMed search for the misspelled "Actea" (rather than the correctly spelled *Actaea*) retrieves three citations.

A practice in the medicinal plant literature, which is often not followed, is that every study should reference the relevant scientific specimen and indicate where the specimen is curated for reference. The voucher itself is more important than the correct identification, as an erroneous scientific name attributed to a voucher can be corrected or amended at a later date.

In accordance with the International Code of Botanical Nomenclature, there is only one accepted scientific name for a taxon. However, Bennett and Balick use black cohosh as a well-known example to which synonyms are applied. The choice of the scientific name depends on the interpretation of taxonomic data by a given specialist. For example, in the treatment of the Ranunculaceae (buttercup family) in *Flora of North America*, separation of the genera *Actaea* and *Cimicifuga* is maintained.[16,17]

Similarly, in the 2001 treatment of the Ranunculaceae in *Flora of China, Actaea*, *Cimicifuga*, and *Souliea*[18-20] are treated separately with the caveat, "Elsewhere (Compton et al., *Taxon* 47:593-634. 1998), *Cimicifuga* has been transferred to *Actaea*. However, for the present account, as in FRPS [*Flora Reipublicae Popularis Sinicae*], one of us (Li) prefers to maintain *Cimicifuga* as distinct."[19]

In the case of black cohosh and its relatives, researchers must be cognizant of relevant synonyms in retrieving scientific papers published in the last 15 years.

Plant names associated with black cohosh and its relatives are easily confused in the scientific literature. Some research groups refer to studied species under the taxonomic concept of *Cimicifuga*, while others embrace the broader generic concept of *Actaea* as defined by Compton and colleagues in their 1998 reclassification.[12] The practical application of the taxonomy is not as easy as simply replacing the genus name *"Actaea"* for *"Cimicifuga"* when referring to species under either genus name.

For example, C. Ma *et al*. (2011) provide methods for authentication and differentiation of *Actaea* species using high-performance liquid chromatography (HPLC) coupled with electrospray ionization time-of-flight mass spectrometry (HPLC-TOF-ESI-MS). The study states that in addition to *A. racemosa*, there are eight more North American species of *Actaea*. However, the authors include both *A. podocarpa* and "*A. americana*," the latter a synonym of no botanical standing for *A. podocarpa*. *Actaea podocarpa* formerly was known as *Cimicifuga americana*, and it appears that in this case the genus name *"Actaea"* was erroneously substituted for *Cimicifuga*. Fortunately, the chemical profiles for *A. podocarpa* and the purported *"A. americana"* in the study are virtually identical. Therefore, there are only eight North American *Actaea* species, rather than nine, as suggested by C. Ma *et al*.[21]

Furthermore, when exploring the historical record, the reader should be aware of additional nomenclature complexities. The genus name "*Macrotrys*," established by C.S. Rafinesque in 1808 as a new designation for *Cimicifuga racemosa*, was subsequently misspelled "*Macrotys*" (omitting the second "r") in several of the eight editions of the popular *Manual of Botany* by Amos Eaton (1776-1842), published from 1817-1840, and widely used as a standard field reference until the mid-19th century. Black cohosh was adopted as a drug by the Eclectic medical movement in the mid-19th century, and the Eclectics nearly universally referred to the drug under the misspelled genus name "*Macrotys*," perpetuating the error of Eaton. The common name black cohosh did not come into widespread use until the late 19th century. Macrotys and black snakeroot were widely used as common names for black cohosh until about 1900.[14,22]

Comments on Names of Source Plants of Chinese Extracts

Various Chinese species of *Actaea* are source plants of the traditional Chinese medicine *sheng-ma* (*shengma*). Three *Actaea*/*Cimicifuga* species are official source plants of *sheng-ma*: *A. heracleifolia* (*C. heracleifolia,* aka *da-san-ye sheng-ma*), *A. dahurica* (*C. dahurica*, *C. dahurica* var. *simplex,* aka *xin-gan sheng-ma*), and *A. cimicifuga* (*C. foetida,* aka *sheng-ma*). *Actaea simplex* (*A. cimicifuga* var. *simplex*, *C. simplex*, *C. foetida* var. *simplex*) is known as *ye-sheng-ma*.

Actaea simplex is the most commonly cultivated Asian species related to black cohosh in American horticulture and an excellent example of the confused nomenclature of black cohosh relatives in commercial trade, extending beyond sourcing of botanical dietary supplement ingredients. *Actaea simplex* is known by numerous botanical synonyms, including "*Cimicifuga ramosa*," which is not a misspelling of "*C. racemosa*." "*Cimicifuga ramosa*" cultivars are widely available as perennials in American horticulture, particularly selections in the "atropurpurea group" which have purple-to-bronze foliage. Cultivar names are expressed as the scientific name, followed by the cultivar designation enclosed in single quotes. For example, one cultivar is *Cimicifuga ramosa* 'James Compton,' named for botanist and taxonomist James Compton, PhD, recent monographer of the genus *Actaea*.[12] To further confuse matters, many nurseries offer "*Actaea ramosa*" bronze-foliage cultivars, even though the name *"Actaea ramosa"* never was published as a scientific name for any plant. Here, the genus name "*Actaea*" simply has been used to replace the genus name *Cimicifuga* with no attempt to determine the correct botanical name for

In the case of black cohosh and its relatives, researchers must be cognizant of relevant synonyms in retrieving scientific papers published in the last 15 years.

Black Cohosh *Actaea racemosa*. Photo ©2013 Steven Foster

* There are varying levels of evidence from clinical trials that may be used to support many of these health uses; mention of these uses here is merely for the purpose of acknowledging the range of use of black cohosh preparations and is not an endorsement or statement of support by the author or publisher of confirmed efficacy.

the plant at hand. A simple Google search for "*Cimicifuga ramosa*" will return numerous sites listing bronze-foliaged cultivars of *A. simplex* as "Cimicifuga racemosa" or "*Actaea ramosa*." This example is highly indicative of the confused understanding and application of binomials in the *Actaea/Cimicifuga* genus nomenclatural complex.

The root of *Vernonia aspera* (Asteraceae; also known as roughleaf ironweed) is an obscure Chinese folk medicine known as *hei-sheng-ma*,[23] which translates to "black cohosh" (*hei*=black). It occurs on open grassy slopes in mountains above 3,000 feet in south China (Guizhou, Hainan, and Yunnan provinces), as well as India, Laos, Myanmar, Nepal, Thailand, and Vietnam, and is known by at least 12 botanical synonyms in six genera.[24,25] A PubMed search using all 13 names in the botanical literature returned no results on scientific studies published on *Vernonia aspera* or any of the synonyms. This author located no reference to *Vernonia aspera* in any of the chemical analytical studies on *Actaea/Cimicifuga* adulteration. There is a virtual dearth of scientific literature on *Vernonia aspera,* yet multiple listings as a source plant of "black cohosh extract" on wholesale Chinese websites are common. Is the plant actually used as a base-material for extract, spiked with triterpenes to make it appear to be a black cohosh extract? Or is this simply yet another case of confused nomenclature lost in translation from Chinese to English on Internet sites?

The AHP monograph on black cohosh makes reference to *guang-dong sheng-ma* as a common substitute for *sheng-ma* in the Asian market.[9] *Serratula chinensis* (Chinese sawwort root, syn. *Rhaponticum chinense*, *Centaurea mossionis*; Asteraceae) is found on grassy slopes, thickets, and forest edges in western Anhui, Fujian, southeast Gansu, north and northeast Guangdong, Guizhou, Henan, Hubei, Hunan, Jiangsu, Jiangxi, south Shaanxi, Sichuan, Yunnan, and south Zhejiang provinces in China.[26] According to Professor De-An Guo, PhD, director of the Shanghai Center for Traditional Chinese Medicine Modernization, *hei sheng-ma* also refers to *Serratula chinensis*, which may be collected by Chinese exporters since it has the same name (in Chinese) as black cohosh. He noted that as far as he can determine, there is no commercial cultivation of *A. racemosa* in China (personal communication to S. Foster and M. Blumenthal, March 25, 2013). The scientific literature on *Serratula chinensis* also is exceedingly sparse. A PubMed search retrieved only one citation — a 2007 study in which Ling *et al*. reported on the isolation and structure of a new cerebroside from the species, the first report of the occurrence of cerebrosides in the genus *Serratula*.[27]

The sheer volume of offerings, prices ranges, varied specifications, and differing species listed as "black cohosh extract" from Chinese sources require that the daunted buyer attempting to source black cohosh work closely with a qualified analytical lab to authenticate black cohosh extracts before securing any supply source.

Sampling of Names from Chinese Wholesale "Black Cohosh Extract Sources"

According to the nomenclature reference AHPA's *Herbs of Commerce,*[28] the only acceptable species to which the common name "black cohosh" applies is *Actaea racemosa* (syn. *Cimicifuga racemosa*). *Herbs of Commerce* is formally recognized in Title 21 of the US Code of Federal Regulations (CFR)[29] as a primary reference for the appropriate labeling of herbal products in the US, and, therefore, non-compliance with this text — unless otherwise scientifically warranted — is a violation of dietary supplement good manufacturing practices (GMPs), and other regulations pertaining to product labeling. According to the same text, Chinese species of *Actaea* (syn. *Cimicifuga*) are required to be identified by the standard common name "Chinese cimicifuga." This name is subsequently required in finished-product labeling, thus clearly distinguishing between Asian and North American species contained in a product. Any designation of a botanical material or finished product in the United States by the common name of "black cohosh" on product labels (and presumably in the supply chain) is required to be *Actaea racemosa* and no other species. To apply the name "black cohosh" to any other species violates the CFR and results in adulteration of the finished product offered to consumers.

Much of the material offered from wholesale sources of Chinese origin appear to be offered as "black cohosh" rather than "Chinese cimicifuga," as listed in *Herbs of Commerce*. An Internet search conducted on Google with the simple search phrase "Black Cohosh Wholesale China" led to a first hit at alibaba.com, which returned 2,440 black cohosh herbal extracts on 77 pages. Searching the landing page for "black cohosh root extract"[30] returned 1,670 herbal extracts listed on 47 pages. Random price ranges for extracts were between $1.00-$300.00/kg, with ranges of availability from various suppliers offered at as little as a few grams per week up to five tons per week. Several plant species under various correct or incorrect spellings of common and or technical names were listed as the source of "black cohosh extract(s)." For example, "ISO9000 & Kosher certificate black cohosh extract," 2.5% triterpenoides (HPLC) of "Cimicifuga romose (L) Nutt." was offered by Sanyuan Jinrui Natural Ingredients Co., Ltd. (Xi'an, Shaanxi, China) at $5-60/kg.[31] Hunan Naturalin Bio-Resources Co., Ltd. (Changsa, Hunan, China), offered 2.5% triterpene glycosides "black cohosh extracts" from "*Cimicifuga foetida* L."[32] Xi'an Aladdin Biological Technology Co., Ltd. (Xi'an, Shaanxi, China) offered "Black Cohosh Extract," citing the Latin name *Vernonia aspera* (Roxb.) Buch.-Ham.[33] This illustrates the myriad offerings encountered in a simple search and represents random samples of 18 different supply source site links out of 38 suppliers listed on just one of 47 pages returned on the alibaba.com website search of "black cohosh root extract." The names mentioned above — "Cimicifuga romose," *Cimicifuga foetida*, and *Vernonia aspera* — were observed on more than one page in this very limited random sample. A follow-up search for "Cimicifuga romose" (an apparent and often repeated misspelling) returned a list of 387 products from 53 suppliers.[34] A search for "*Cimicifuga foetida*" returned 121 products from 24 suppliers, most of which also called the products offered "black cohosh extract."[35] A follow-up search of "*Vernonia aspera* extract" returned a list of 17 products from 11 suppliers.[36] In all 17 instances, the name "*Vernonia aspera* extract" was associated with products labeled as "black cohosh extract." As stated, none of the aforementioned Chinese species are acceptable as "black cohosh" and clearly are represented as adulterated products under Title 21 of the CFR.†

Black Cohosh *Actaea racemosa*. Photo ©2013 Steven Foster

The Price of Authentic North American Black Cohosh

Price differences between authenticated North American black cohosh and Chinese species sold labeled as "black cohosh" provide the obvious incentive for economic adulteration. Estimates suggest that between 300,000-380,000 lbs (136,078-172,365 kg) of wild-harvested crude, dried, whole black cohosh root enter the wholesale trade from the US (as of the 2011 season) with prices from supplier/dealer to manufacturers/processors ranging from $4.50-$7.50/lb ($9.92-$16.54/kg). Some *cultivated* material is sold in small lots, mostly to small manufacturers at about $8.00/lb ($17.80/kg), but is not believed to represent a significant percentage of the wholesale black cohosh supply. (Fletcher E., email to S. Foster and M. Blumenthal, April 2-5, 2013).

Cultivated wholesale black cohosh root for the medicinal herb trade is not economically feasible to produce, at least not at the present time. The time frame for growth from seed to production of roots of large enough size for the medicinal market is estimated at six-to-eight years, which would require at least doubling and perhaps tripling the price compared with wild-harvested material to recoup the investment in time and inputs. At this point, cultivated material — compared with the relative abundance and much lower price of wild-harvested material — provides little incentive to commercial growers except in vertically integrated operations with a desire or need to control supply sources. (Fletcher E., email to S. Foster and M. Blumenthal, April 2-5, 2013).

Chinese sources sell powdered material or extract to the US market, rather than crude raw material. Authenticated black cohosh extract at $50.00/kg can be expected to be three-to-four times the price of Chinese-supplied extract (averaging around $15.00/kg), depending upon quantities. Prices paid for Chinese-supplied black cohosh ranged from $6-$8.50/kg (including shipping) while US-supplied black cohosh ranges from $14.50-$16.50/kg. Obviously, prices vary considerably based on root quality, form (whole, cut, powdered), and quantities purchased, but the overall trend shows an economic adulteration incentive with the price of Chinese material running at about 25-30 percent, or in some cases, much less, of that of authenticated black cohosh in wholesale trade (Fletcher E., email to S. Foster and M. Blumenthal, April 2-5, 2013; Wanzer C., email to M. Blumenthal, April 4 and 5, 2013).

† Per 21 CFR 101.4(h): "The common or usual name of ingredients of dietary supplements that are botanicals (including fungi and algae) shall be consistent with the names standardized in [the American Herbal Products Association's] *Herbs of Commerce,* 1992 edition, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51."

Habitat and Conservation

Black cohosh occurs in moist, mixed deciduous eastern North American forests and forest margins, often in mountainous terrain from Massachusetts south to Georgia, west to northwest and north central Arkansas and the adjacent Ozarks of Missouri, north through the Ohio River Valley to southern Ontario. Although not of significant conservation concern at the national level, at the extremities of the plant's natural range it may be considered rare at the state level.

Conservation concerns expressed by various groups including the US National Park Service, World Wildlife Fund, United Plant Savers, and others prompted the US Fish and Wildlife Service (USFWS) to request information and recommendations for species to consider for changes to CITES (Convention on International Trade in Endangered Species of Wild Fauna and Flora) in the US *Federal Register* in June of 2001.[37] At the time, USFWS was considering recommending black cohosh for a CITES Appendix II listing, which may have monitored and/or restricted black cohosh in international trade.

AHPA responded to the USFWS request for information with a detailed commentary on the suspected over-harvest of black cohosh root for export.[38] Subsequently, USFWS published a notice in the *Federal Register* in April of 2002 stating that it would not seek an Appendix II listing, but that it intended to review and consider listing US native species of *Cimicifuga* (*Actaea*) in Appendix III.[39] CITES Appendix III includes species listed by one member country in which assistance in controlling trade is sought from other CITES Parties, in which case trade would be permitted only among CITES Parties if the member country that listed the species issued an appropriate export permit and certificate of origin. However, no action was taken at the CITES Conference of the Parties (COP 12) held in Santiago, Chile, in November of 2002. As of March 2006, active consideration to list black cohosh and its relatives was withdrawn by the USFWS, though the agency has been monitoring and will continue to monitor status.[40]

The information provided by AHPA in response to the initial request for information and recommendations appears largely responsible for the lack of action taken to list black cohosh to a CITES Appendix. In the past decade, Remifemin-manufacturer Schaper & Brümmer GmbH & Co. KG has established large-scale commercial production of black cohosh in Germany in order to better control and secure its supply source. The company's production quantity is unknown and not reflected in trade data, though this commercial production may contribute to an overall trend of stabilization in wild-harvested tonnage and decreased conservation concerns from wild harvest.

Ed Fletcher of Strategic Sourcing Inc., an experienced trader and consultant on North American medicinal plants and a supplier of wild-harvested and cultivated black cohosh rhizomes/roots, observes that habitat depletion is the most detrimental factor to current wild populations of black cohosh. He believes that managed stands of wild black cohosh regenerate adequately to be self-sustaining.

Black Cohosh *Actaea racemosa.* Photo ©2013 Steven Foster

Black Cohosh *Actaea racemosa.* Photo ©2013 Steven Foster

Population sustainability is achieved in part by high seed production in wild populations and relatively high germination rates, which helps to ensure the ability of populations to recover from harvest impacts (personal communication, September 6, 2011).

Trade Data on Black Cohosh

In a detailed analysis of black cohosh rhizome trade from the US, Brinckmann (2010)[41] provided information on production scenarios, conservation status, trade volume, and market prices, along with information on quality expectations and pharmacopeial definitions. One of the problems in monitoring international trade in black cohosh is that the commodity does not have a unique 10-digit tariff code assigned to it under the Harmonized Tariff Schedule of the United States (HTSUS). The only estimates of annual trade volume and percentage of cultivated and wild-harvested black cohosh come from AHPA's annual tonnage surveys of member companies that are primary raw material producers (direct buyers from point of origin) with data on up to 26 wild-harvested botanical commodities collected from 1997 to 2010 (Table 1).

Retail sales ranking of black cohosh products in the food, drug, and mass market channel as

Table 1. Black Cohosh Estimated Annual Trade Quantities in North America Dry Weight in kg

1997-2010

Year	Estimated quantity (kg) from cultivation	Estimated quantity (kg) from wild-collection
1997	0	102,967
1998	16,071	329,304
1999	1,179	65,938
2000	68	53,453
2001	2,958	80,596
2002	128	76,856
2003	186	144,309
2004	1,502	144,575
2005	3,143	61,857
2006	925	139,478
2007	1,012	155,932
2008	724	129,809
2009	629	76,509
2010	4,473	142,743

Source: Aggregate data from AHPA tonnage surveys as reported by Brinckmann (to 2005)[48] and AHPA.[49]

well as the health and natural foods channel in the US have remained relatively stable over the past six years, as reflected in trade data summarized in *HerbalGram*'s annual Herb Market Reports (Tables 2 and 3).

Table 2. Black Cohosh Dietary Supplement Product Sales Ranking, Sales Estimates, and Percent of Change over Previous Years in Food, Drug, Mass Market (FDM) Channel in US
2006-2011

Year	Sales Rank	Retail Sales	% ± Over Previous Year
2011	8	$10,319,990	+9.85
2010	8	$9,303,047	+14.34
2009	10	$8,123,878	+0.29
2008	10	$8,122,758	-7.07
2007	7	$8,641,608	-0.47
2006	8	$8,682,563	0

Data do not include sales in WalMart stores. Information supplied for Food, Drug, and Mass Market retail stores, as compiled by Symphony IRI and published in the American Botanical Council's annual Herb Market Report in *HerbalGram*.[50-54]

Table 3. Black Cohosh Dietary Supplement Product Sales Ranking, Sales Estimates, and Percent of Change over Previous Years in Health and Natural Foods Channel in US
2008-2011

Year	Sales Rank	Retail Sales	% ± Over Previous Year
2011	19	$3,848,203	+2.5
2010	-	(not ranked in top 20)	
2009	17	$3,645,883	+3.23
2008	18	$4,915,972	-4.11

Source: American Botanical Council's annual Herb Market Report in *HerbalGram*. [51-54]

Potential Confusion of North American *Actaea/Cimicifuga* Species

Accidental *A. racemosa* adulteration or inadvertent admixture to commercial lots may occur with several North American *Actaea* species that share the same habitat and whose ranges overlap. *Actaea podocarpa* (syn. *C. americana*, *A. americana*) occurs in a narrow range in the central Appalachian mountains from Pennsylvania south to Georgia. Appalachian bugbane (*A. cordifolia,* syn. *C. cordifolia*, *C. rubifolia, C. racemosa* var. *cordifolia*, *A. rubifolia*) has a narrow range limited to a few counties in Pennsylvania, Virginia, Tennessee, Alabama, Kentucky, and southern Illinois and Indiana. *Actaea pachypoda* and *A. rubra* also share overlapping ranges with *A. racemosa*. All five species are known to occur in the same habitat, often in sterile populations, with few distinguishing features if flowers and/or fruits are not available. This could result in unintentional admixture of one or more of the above species in commercial lots of *A. racemosa*.[14]

Fletcher noted that, in practical terms in Appalachia, *A. podocarpa* (yellow cohosh) is the species that most closely resembles black cohosh. Wildcrafters pass over other *Actaea* species because the roots/rhizomes are smaller, and they know that buyers will not purchase other *Actaea* species. However, once the roots are dry they become visually more difficult to differentiate (personal communication, September 6, 2011).

In the AHP Black Cohosh Rhizome monograph, Upton *et al*. (2002) suggest that yellow cohosh (*A. podocarpa*) is unintentionally but commonly mixed with *A. racemosa* based on similarities of above-ground morphological features. The AHP monograph provides a table showing unique visual features that provide distinction between *A. racemosa* and *A. podocarpa* fruit, seed, pistils, pedicels, bracts, and staminodea. When fresh, black cohosh root is black and yellow cohosh root is yellow, though once dried they are more difficult to differentiate. Also, *A. podocarpa* blooms about three weeks later than *A. racemosa*.[9]

DNA Analysis and Barcoding

Several DNA studies on *Actaea* have been published distinguishing *A. racemosa* from other *Actaea* species, as well as increasing awareness of geographical and chemical diversity in the genus.

In a comprehensive paper explaining DNA barcoding as it relates to accuracy of identification of medicinal plants published in *HerbalGram* 97, Y.C. Ma *et al*. of the Canadian Phytopharmaceutical Corporation,[48] suggest that DNA barcoding is emerging as a useful methodology in the quality control toolbox to help reduce misidentification and adulteration of medicinal plants. The practical application of DNA barcoding to plant identification is an evolving field, circumscribed by key limiting factors such as standardization minimalism and scalability. In animals, a fragment of a single gene (cytochrome *c* oxidase 1) is the accepted standard for ease of species differentiation. However, no single region of plant DNA provides universal sequence quality and species discrimination of plants, leading to development of various proposed methods or a combination of methods to correctly identify plants based on their DNA barcodes.

Y.C. Ma *et al*. explain that a short region of DNA is used to identify species in DNA barcoding. First, a small sample of DNA has to be extracted from the specimens. Second, the selected barcode region undergoes polymerase chain reaction (PCR) amplification. The PCR result is purified and sequenced; then, the DNA sequence is compared to a

Black Cohosh *Actaea racemosa.* Photo ©2013 Steven Foster

library/database to identify the species.

Researchers in China at the Institute of Medicinal Plant Development (IMPLAD) in Beijing and the Institute of Chinese Medicine at The Chinese University of Hong Kong have taken the lead internationally in developing DNA barcoding of botanical ingredients including medicinal plants and their adulterants. The Medicinal Materials DNA Barcode Database,[49] for example, covers 1,658 plant species. The 2015 *Pharmacopoeia of the People's Republic of China* likely may be the first national pharmacopeia to contain detailed DNA protocols for authentication of herbal medicines.

In order to distinguish among sympatric eastern North American species of *Actaea*, several research groups have effectively applied DNA fingerprinting methods. Xu *et al*. (2003) found that random amplified polymorphic DNA (RAPD) analyses could distinguish *A. racemosa*, *A. podocarpa,* and *A. cordifolia* when no powdered plant materials were available.[50]

Zerega *et al*. (2002) used Amplified Fragment Length Polymorphism (AFLP) DNA fingerprinting to analyze black cohosh in relationship to its relatives with overlapping ranges. The method was applied to commercial black cohosh products, and, in two products, verification of the presence of *A. racemosa* was confirmed along with the absence of other eastern North American *Actaea* species. However, use of this method was unable to verify the presence or absence of *Actaea* species in black cohosh tea bags and coated tablets. Variables such as rhizome temperature drying, storage conditions, processing techniques, age, and storage quality of finished products could have individually or collectively contributed to the degradation of DNA, with loss of AFLP markers, highlighting the limitation of the method.[51] The results also supported the uniting of *Cimicifuga* with *Actaea* by Compton *et al*.,[12] and suggest that the morphologically dissimilar *A. racemosa* and *A. pachypoda* are the most closely related eastern North American *Actaea* species in terms of genetics.

Pate *et al*. (2012) applied isolating microsatellite DNA loci to develop molecular markers for *A. racemosa* from living specimens throughout the plant's geographical range. The aim of the research was to measure genetic diversity across the species' range as a tool to examine potential genetic depletion in the southeastern United States, and provide a context for detecting possible genetic variations in triterpene glycoside production. The characteristics of seven microsatellite regions provide a comparative genetic library for use in the future assessment of population structure and genetic relationships, which also could aid in assessing genetic variables for active compound production.[52]

Baker *et al*. (2012) applied another method of identifying two *matK* nucleotides from the DNA sequences (barcodes) of black cohosh that consistently and unambiguously distinguishes black cohosh from all related species. In a sampling of 40 dietary supplement products labeled as "black cohosh" arbitrarily purchased on the Internet and from New York metropolitan-area stores, the researchers found that of 36 samples sequenced, 27 (75%) exactly matched black cohosh. Nine samples (25%) had sequences identical to three Asian *Actaea* species (*A. cimicifuga*, *A. dahurica*, and *A. simplex*). As noted above, *Actaea simplex* is widely available in American horticulture, but often mislabeled, adding to potential confusion.

Significantly, none of the samples studied contained any North American *Actaea* species other than *A. racemosa*, suggesting that wild collectors, buyers of wild-collected North American material, and their customers' quality control procedures are achieving success at maintaining correct identity of authentic *A. racemosa* in North American-sourced black cohosh supplies.

Four dietary supplements could not be identified using the lab's PCR amplification protocol, presumably because the DNA was degraded, possibly when heat was applied during processing. Nevertheless, the method described in the Baker *et al*. paper using *matK* sequence supplemented by nrITS2 can consistently and unambiguously differentiate black cohosh, assuming that the DNA is not degraded.[53‡]

Chemical Differentiation of *Actaea* species

Various studies on the chemical constituents of black cohosh reveal that the two principal compound groups in the plant are triterpene glycosides (at least 43 reported to date) and polyphenolic derivatives, which have been the major focus of analysis and characterization of black cohosh products. However, in an effort to conclusively identify standardization methods based on active compounds and biological activity, the late Professor Farnsworth's research group at UIC reported new potential bioactive compounds from black cohosh. Fabricant *et al*. (2005), as part of an effort to produce a standardized, definable extract for use in the UIC black cohosh clinical trials, reported on the isolation and characterization of a new cyclic guanidine alkaloid, cimipronidine, the first guanidine isolated from a plant in the Ranunculaceae.[54] Gödecke *et al*. (2009) isolated and characterized three new guanidine alkaloids including cylo-cimipronidine and cimipronidine methyl ester (both congenors of cimipronidine), and a new alkaloid given the trivial name dopargine, a derivative of dopamine. These and other compounds, including 3-hydyroxytyrosol 3-*O*-glucoside, may contribute significant biological activity in polar fractions of an extract produced for use in clinical trials, and they are being researched further for their serotonin receptor pathways, and possible central nervous system and antioxidant activity.[55]

With respect to polyphenolic compounds, in 2006, Nuntanakorn *et al*. reported on the identity of 17 polyphenols including hydroxycinnamic acid derivatives (caffeic acid, ferulic acid, and isoferulic acid); fukiic acid derivatives (fukinolic acid and cimicifugic acids A and B); and piscidic acid ester derivatives (cimicifugic acids E and F). In addition, they reported — for the first time — the presence of six additional phenolic compounds including protocatechuic acid, protocatechualdehyde, *p*-coumaric acid, 1-isoferuloyl-β-D-glucopyranoside, ferulate-1-methyl ester, and cimicifugic acid D. They also isolated two new compounds, a lignin — actaealactone — and a phenylpropanoid ester derivative — cimicifugic acid G — with structures determined based on nuclear magnetic resonance (NMR) spectrometry analysis.[56]

In 2007, Nuntanakorn *et al*. published a method to distinguish among various eastern North American *Actaea* species based on phenolic component fingerprints. A reversed-phase high-performance liquid chromatography (RP-HPLC) method with diode array detection (DAD) is useful for distinguishing the eastern North American *Actaea* species *A. pachypoda*, *A. podocarpa*, *A. racemosa*, and *A. rubra* based on polyphenolic components. Described as a simple, reliable, and convenient method less complex than distinguishing triterpene glycoside fingerprints, the method provides qualitative and quantitative polyphenolic fingerprints to reliably distinguish these four species. The method was validated with respect to sensitivity, linearity, precision, accuracy, and recovery.

Black Cohosh *Actaea racemosa*. Photo ©2013 Steven Foster

The eight polyphenolic compounds detected included caffeic acid, ferulic acid, isoferulic acid, fukinolic acid, and cimicifugic acids A, B, E, and F. *Actaea racemosa* contains all eight polyphenolic compounds. *Actaea rubra* has a similar phenolic profile to *A. racemosa*, but different ratios of polyphenols with higher levels of cimicifugic acids A and B as the predominant polyphenols, while fukinolic acid is the most abundant polyphenol in *A. racemosa*. Cimicifugic acid F was not found in *A. rubra*. In *A. pachypoda*, isoferulic acid and cimicifugic acid A are the only two predominant polyphenols. *Actaea podocarpa* contains cimicifugic acids A and B as the only two predominant polyphenols. The sympatric eastern North American species *A. cordifolia* (syn. *C. cordifolia*, *C. racemosa* var. *cordifolia*, *C. rubifolia*) does not seem to have been tested. An additional eight populations of black cohosh from New York to North Carolina and Tennessee were examined, all of which had similar profiles of polyphenolic constituents. Replication of the method could be applied to more collections of North American *Actaea* species.[57]

Further Analytical Tools and Methods for Authentication

The analytical tools and methods to assure that black cohosh (*A. racemosa* syn. *C. racemosa*) is properly identified are numerous, precise, and widely known to experts in the herb trade and the natural products research community. A combination of the use of several analytical methods may be necessary for proper authentication of black cohosh and to rule out economic adulteration or inadvertent admixture of related species.

In its black cohosh guidance document, AHPA advocates the relatively inexpensive method of high-performance thin-layer chromatography (HPTLC), citing the methodology of Verbitski *et al*. (2008)[58] for authentication of black cohosh in comparison to other North American species of *Actaea/Cimicifuga*. The HPTLC methods of Ankli *et al*. (2008) of CAMAG Laboratories[59] in Switzerland are suggested for detecting adulteration of black cohosh from Chinese species of *Actaea/Cimicifuga*. Members of the HPTLC Association can access further details of these methods through the organization's website (no open access).[60]

C. Ma *et al*. (2011)[21] provide further methods for authentication and differentiation of *Actaea* species, using HPLC coupled with the HPLC-TOF-ESI-MS technique. They identified 15 chemical markers including three marker compounds that were unambiguously identified using authentic standards, and an additional 12 marker compounds tentatively identified by fragmentation patterns when compared with previously reported data.

The analytical methods described in the paper that distinguish 15 marker compounds inform differences among four types of *Actaea* classified as follows: (1) species other than *A. racemosa*, (2) Asian species of *Actaea*, (3) *Actaea racemosa*, and (4) North American species other than *A. racemosa*.

Of note, three cimifugin derivatives and a 16,23-diketoshengmanol class triterpene marker were found useful to differentiate species other than *A. racemosa*. For example,

‡Those readers interested in a better understanding of the value and limitations of DNA barcoding are encouraged to visit the Barcode of Life website (www.barcodeoflife.org), which contains both introductory and technical details, along with many additional information resources on species identification via DNA barcoding, with links to the Barcode of Life Database (maintained by the University of Guelph in Ontario). See, for example: Wallace LJ, Boilard SMAL, Eagle SHC, Spall, JL, Shokralla S, Hajibabaei M. DNA barcodes for everyday life: Routine authentication of Natural Products. *Food Research International*. 2012;49(1):446-452.

the cimifugin derivative prim-*O*-cimifugin was present in Asian and North American species except for *A. laciniata*, *A. podocarpa,* and *A. racemosa*; therefore, the presence of that compound in a "black cohosh" product would indicate adulteration.

The alkaloid cimicifugaine (syn. cimicifine A) was found to be unique to Asian species of *Actaea* (including *A. heracleifolia*, *A. mairei*, *A. dahurica*, and *A. yunnanensis*). The presence of this alkaloid is useful for identifying the presence of Asian *Actaea* species, and if found in a product labeled as containing "black cohosh," would again indicate adulteration.

A single compound, 12 β,21-dihydroxycimigenol-3-*O*-L-arabinoside, was found in high concentration in *A. racemosa*, but was absent from all other North American and Asian *Actaea* species tested; therefore, it is useful in detecting unadulterated *A. racemosa* product.[21]

Another compound, cimigenol-3-*O*-a-L-arabinoside (syn. cimiracemoside C, cimicifugoside M), was reported by He *et al*. (2000) to be unique to *A. racemosa* and hence reported to be a useful marker compound for *A. racemosa*.[61] However, Ma *et al*., using the highly sensitive methods in the time-of-flight mass spectrometry analysis, detected the compound in three additional North American species and one variety of *Actaea*, as well as three Asian species of *Actaea*.

In addition, other published analytical methods for unambiguous identification of black cohosh include the HPLC method of Avula *et al*. (2007).[62] Avula *et al*. (2009) provide a UPLC/UV/ELSD (ultra performance liquid chromatography/ultra-violet/evaporative light scattering detection) method and identification by UPLC-MS (ultra performance liquid chromatography/mass spectrometry).[63] The HPLC-photodiode array (PDA)/mass spectrometric (MS/ELSD) method of He and colleagues (2006) provides more guidance.[64] A LC/TIS/MS (liquid chromatography/turbo ion spray/mass spectrometry method) developed by Wang *et al*. (2006) presents fingerprints of six commercial black cohosh products along with six related Asian species. The method produces LC/MS fingerprints that provide reliable and reproducible methods useful for identification of *Actaea*/*Cimicifuga* species and validation of commercial products.[65]

Gafner *et al*. (2006) noted that the evaluation of chemical fingerprinting using a combination of techniques is especially useful in the quality control of black cohosh, since the majority of triterpene glycosides of *A. racemosa* also occur in several other *Actaea* species. An identification procedure based on a few marker compounds may not be enough to rule out every adulterant. They compared HPLC-UV, HPLC-MS, HPLC-ELSD, and HPTLC fingerprints of five *Actaea* species (*A. racemosa*, *A. rubra*, *A. pachypoda, A. podocarpa*, and a Chinese *Actaea* species sold as *A. heracleifolia* by the supply source). HPTLC gives good separation of phenolics and triterpene glycosides, but *A. rubra*, *A. podocarpa*, and *A. pachypoda* showed very similar fingerprints to *A. racemosa*, leading the authors to conclude that it was difficult to determine identification of *A. racemosa* by HPTLC alone. HPLC-UV showed distinct differences between *A. racemosa* and the Chinese *Actaea* species, but there was little distinction between *A. racemosa* and *A. podocarpa*, plus *A. rubra* and *A. pachypoda* exhibited almost exactly the same HPLC-UV trace. However, HPLC-ELSD coupled with HPLC-MS provided unambiguous identification of *A. racemosa*, according to the authors. None of the techniques were able to unambiguously distinguish between the two closely-related North American species *A. rubra* and *A pachypoda*.[66]

Dr. Kennelly's research group at Lehman College at the City University of New York, with collaborating researchers at various institutions, has published a series of papers on the identity of black cohosh components and authentication.[§] Remarkably, Jiang *et al.* (2005) found that an 85-year-old black cohosh specimen collected in 1919 by H.H. Rusby had comparable quality and quantities of four triterpene glycosides and six phenolic constituents, compared with modern plant material, confirming the potential stability of those constituents in storage.[67] Jiang *et al*. (2006), analyzed 11 commercial products from the US labeled as black cohosh using HPLC-PDA+LS(SIM) and found that three products contained the marker compound cimifugin (and not cimiracemoside C), indicating they contained Asian *Actaea* species rather than authentic black cohosh, and one product contained a mixture of black cohosh and an Asian *Actaea* species.[68] A more recent paper (Jiang *et al*., 2011) from this same group used HPLC/LC-MS analysis to distinguish HPLC fingerprints for both polyphenols and triterpene glycosides from samples of 15 *Actaea* species including eight North American species and seven Asian species. Of note, cimifugin was detected in all Asian species tested as well as three American species of *Actaea*, but was absent from *A. racemosa*, as well as three closely related North American species (*A. podocarpa*, *A. pachypoda*, and *A. rubra*).[69]

In addition, the United States Pharmacopeial Convention (USP) has published authentication methods for black cohosh.[70] Health Canada's monograph,[71] the EC European Medicines Agency monograph,[72] and related documents all provide further guidance for quality assessment, authentication, and use guidance for black cohosh products.

Products Labeled "Black Cohosh" and Alleged Liver Toxicity

Since 2002, beginning with several case reports from Australia, presumed herb-induced liver injury has been linked to products labeled as containing black cohosh. Reactive alerts by regulatory bodies, when assessing causality, gave preference to quantity of cases over quality of case data.[73] On November 22, 2004, the NIH, NIH National Center for Complementary and Alternative Medicine (NCCAM), and the NIH Office of Dietary Supplements (ODS) convened a workshop on the safety of black cohosh in clinical studies in response to the case reports of hepatotoxicity.

[§]A collaborating botanist who co-authored many papers with Dr. Kennelly's group, Timothy Motley, PhD, the J. Robert Stiffler Professor of Botany at Old Dominion University, died at age 47 on March 28, 2013. A tribute article is available on page 77.

The workshop brought together experts active in multidisciplinary research on black cohosh to gain a better understanding of reported hepatotoxicity in humans and focused on issues relative to NIH-funded studies on black cohosh. The late Professor Farnsworth, citing research from his laboratory at UIC, underscored that there was increasing concern that some of the black cohosh products marketed in the US may not be genuine black cohosh but one (or more) of the Chinese *Actaea* species instead. Consensus was expressed that, given variables in preparations and possible adulteration and/or contamination, NIH grant recipients should have allowable budget costs for verification of research materials. One of the 40 participants at the workshop, Wolfgang Wuttke, MD, of the University of Göttingen in Germany — and principle investigator on several clinical trials on Klimadynon — expressed that his reviews of the black cohosh clinical literature found few if any effects on the liver, and was surprised at the level of concern about black cohosh-associated hepatotoxicity in the US.[74]

Australia's Therapeutic Goods Administration (TGA) was the first regulatory agency to require a warning label for black cohosh products. In 2005, TGA reviewed the safety of black cohosh in relation to possible cases of liver toxicity that at the time included 47 international case reports — nine of which were from Australia. As of February 2006, TGA required black cohosh products to include the following label statement: "Warning: Black cohosh may harm the liver in some individuals. Use under the supervision of a healthcare professional." Following the initial safety review, TGA convened an expert advisory group that concluded that there appears to be an association with products labeled as "black cohosh" and liver disease, but it was very rare.[75] A revised warning stated, "In very rare cases, black cohosh has been associated with liver failure. If you experience yellowing of the skin or eyes, dark urine, nausea, vomiting, unusual tiredness, weakness, stomach or abdominal pain, and/or loss of appetite, stop using this product and see your doctor."[76]

In July of 2006, the UK's Medicines and Healthcare Products Regulatory Agency (MHRA) followed with a suggested product-label warning in conjunction with a public statement by the European Agency for the Evaluation of Medicinal Products/Herbal Medicinal Products Committee (EMEA/HMPC) advising patients and healthcare professionals to be aware of the liver toxicity linked to black cohosh-labeled products. Of the 42 poorly documented case reports evaluated in the world literature, a temporal causality association was made in four cases.[77] Health Canada issued a brief notice in a July 2005 issue of the *Canadian Adverse Reaction Newsletter* encouraging healthcare providers, manufacturers, and the public to be aware of international reports of liver toxicity associated with black cohosh.[78] A follow-up consumer advisory about a possible link between health products containing the herbal medicine black cohosh and liver damage was issued on August 18, 2006.

Continued media reports and regulatory agency warnings regarding the possible association of black cohosh and hepatotoxicity led to the inevitable — lawsuits. Grant and Beck v. Pharmavite and Nutraceutical Corporation involved a case of a 50-year-old woman who claimed to take 500 mg daily of a black cohosh product before the onset of jaundice, leading to a diagnosis of autoimmune hepatitis. The patient required a liver transplant. The case was reported by Levitsky *et al*. in a 2005 issue of *Digestive Diseases and Sciences*.[79] An erratum to the paper was published in the same journal in 2008.[80] One of the authors, Michael F. Sorrell, MD, a gastroenterologist, was one of the treating physicians of co-plaintiff Susan M. Grant, and was retained as an expert witness. According to court documents, only after Dr. Sorrell was retained as an expert witness did he submit a report on Grant's case for publication, which allegedly linked her liver disease to black cohosh. The published case report included a statement that the patient "did not drink alcohol or use illicit drugs, and was not taking any medications, including other herbal medications, acetaminophen [and] nonsteroidal anti-inflammatory drugs."[81] However, the plaintiff's testimony did reveal that she regularly consumed wine, used ibuprofen (an NSAID) on a regular basis, and was prescribed the antiviral drug valacyclovir, all of which may contribute to liver disease. The court granted the defendants a summary judgment resulting in dismissal.[81,82]

A June 26, 2007 press release from the USP announced that the USP Dietary Supplements Information Expert

Black Cohosh *Actaea racemosa.* Photo ©2013 Steven Foster

Committee (DSI-EC) voted to require new labeling suggesting a potential link between black cohosh and liver damage. A proposed Interim Revision Announcement with the cautionary statement for black cohosh was released in *Pharmacopeial Forum* 33(5), for a 60-day public comment period.[83]

In a press release dated January 11, 2008, AHPA urged USP to drop label cautions on black cohosh, noting the following: (1) "USP has not considered the full range of products that may contain a variety of different forms of black cohosh or that the proposed caution is actually warranted for all dosages and use patterns," and (2) "That the need for a cautionary statement was based on an inappropriately narrow review of case reports, which without supportive data are insufficient to justify the proposed cautionary labeling."[84]

In 2008, the USP DSI-EC published a thorough review of alleged black cohosh hepatotoxicity case reports, and regulatory actions and reactions. The extensive review of adverse event reports (AERs) by Mahady *et al*.[82] stated that the DSI-EC observed that the link between black cohosh and liver damage reports were weak and of uncertain causality. Weaknesses of reviewed data found incomplete case information and unknown products, potentially confounding variables such as the use of alcohol and other medications, and preexisting liver disease risk factors. Despite these and other limitations on available data, DSI-EC decided to reclassify black cohosh as "Class 2" for the purposes of a USP black cohosh monograph, requiring a label caution stating the following: "Discontinue use and consult a healthcare practitioner if you have a liver disorder or develop symptoms of liver trouble, such as abdominal pain, dark urine, or jaundice." The label caution applies only to products that are represented as conforming to specifications of an official *USP-NF* monograph.[82,85]

All of the identification and authentication scientific tools necessary to distinguish authentic black cohosh from any other plant materials of any origin are readily available.

Hepatotoxicity of Commercial Products Labeled as Containing "Black Cohosh" Linked to Plant Species Misidentification

Despite numerous cases reports of hepatotoxicity linked to products labeled as containing black cohosh, with at least 82 cases reported worldwide as of early 2010, causality has remained controversial. A report associating hepatotoxicity from commercial products labeled as containing black cohosh linked to plant species misidentification was presented in a poster session by Robin J. Marles, PhD, and colleagues of various branches of Health Canada, on March 23, 2010, at a symposium titled "Developments in Botanical Dietary Supplements Research from 1994 to Today," organized by the UIC College of Pharmacy, in honor of the late Professor Farnsworth's 80th birthday.[86] By March, 2010, Dr. Marles and colleagues at Health Canada reported that the agency under Canadian regulations had licensed at least 78 natural health products (NHPs) containing black cohosh and that an unknown number of additional unauthorized products on the market had yet to come into compliance with NHP regulations.

Dr. Marles and colleagues obtained the same lots of black cohosh products from retail outlets and from the manufacturer of four products of the same brand of black cohosh-labeled products, including a product labeled as containing only black cohosh, along with three additional combination products produced by the manufacturer. The products had been linked to probable adverse liver reactions. Actein, 23-epi-26-doexyactein, and black cohosh powder reference standards were obtained from USP. Cimiracemoside C and cimifugin were purchased from ChromaDex (Santa Ana, CA). LC-MS (liquid chromatography-mass spectrometry) with a photodiode array detector (PDA) was used to analyze the products. Health Canada's analysis of three products, and the manufacturer's analysis of a fourth product, all showed there was no authentic black cohosh in the products when compared with chemical reference standards. The probable adulterant was reported to be *A. cimicifuga* (*C. foetida*), but their raw material supplier reportedly believed it to be *A. dahurica* (*C. dahurica*) based on adjacent warehouse storage of the two Chinese species. Again, these products were associated with cases of probable adverse liver reactions.

After the testing was completed, Dr. Marles *et al.* reported that Health Canada contacted all licensees for black cohosh products, of which 52 were found to have used an appropriate authentication method [not characterized in the poster in relation to the licensees' method(s)], seven licensees requested cancellation of their license, five did not provide enough information to determine compliance, and two did not respond. There were 11 licensees using the same third-party laboratory that was reported to be using an non-validated method returning false positive results.[86]

Painter *et al*. (2010) reported on Canadian products linked to six cases of liver toxicity associated with products labeled as black cohosh. The products were analyzed according to methods described by Dr. Marles and colleagues and were found to contain *Actaea* species other than black cohosh. In two other cases of purported black cohosh liver toxicity connected with products unlicensed by Health Canada, the products connected with the cases were not obtained for chemical analysis. They suggested greater vigilance in reporting liver reactions of products labeled as containing black cohosh.[87]

In June 2007, the NIH ODS convened a workshop on the current state of knowledge for black cohosh in Gaithersburg, Maryland. A summary of workshop results by Betz *et al*. (2009) noted that in contrast to adverse event reports, clinical trials and other human studies involving more than 3,000 subjects, there was not a single report of serious liver problems in any of the trials. In two cases, mildly elevated liver enzymes were reported but judged to be clinically insignificant.[88]

In a detailed, vigorous causality assessment — using a diagnostic algorithm — of the four cases of alleged black cohosh liver toxicity suspected by EMEA/HMPC, Teschke *et al*. (2009) found no evidence for the causal association between black cohosh and liver injury.[89] An analysis and review of the quality and causality of all published case reports plus spontaneous reports of alleged black cohosh toxicity assessed by the scale of the Council for the International Organizations of Sciences (CIOMS) showed lack of causality for black cohosh in all cases. In this review, Teschke and colleagues concluded that true black cohosh may not produce an overt risk of hepatotoxicity, but quality problems in some products may require additional regulatory quality specifications. They wrote that the focus should be on quality specifications to ensure that any problems of impurities, misidentifications, and adulteration of black cohosh products are identified.[73,89]

A review of adverse events associated with black cohosh products was conducted by Borrelli and Ernst (2008),[90] which found that clinical studies suggest black cohosh to be safe; the authors noted that case reports for which causal attribution is problematic require urgent further investigation.

Conclusions

Numerous monographs such as those produced by AHP, USP, Health Canada, and other authoritative official and non-official organizations provide the details necessary for unambiguous authentication of genuine North American black cohosh (*Actaea racemosa,* syn. *Cimicifuga racemosa*) using relatively simple organoleptic, macroscopic, and microscopic classical pharmacognosy methods, coupled with relatively inexpensive and widely available chemical analytical methods such as HPTLC. AHPA offers a guidance document on its website with suggestions to industry of reliable, dependable methods with references to readily available literature. In addition, AHPA provides sources for the availability of reference compound standards, as well as member companies that can supply chemical reference standards, botanical voucher specimens, or commercial labs with proven and known expertise to unambiguously authenticate black cohosh raw material and extracts. Depending upon the condition of raw material, DNA authentication methods also are available. In addition, more expensive, sophisticated, and perhaps less widely available chemical analytical methods using the latest technologies delivering unambiguous information, identification, and authentication have been published in the chemical analytical literature in the last 15 years, especially since 2006.

Beginning in 2002, case reports, many of which are inadequately documented, have appeared in the medical literature associating potential hepatotoxicity to products labeled as containing black cohosh. Suspicions arose that those cases may be associated with adulteration (perhaps with Asian species of *Actaea/Cimicifuga*), but in a vast majority of such reports, the alleged offending product was not retained nor were its contents analyzed by a competent phytochemist. A 2010 report by Dr. Marles and colleagues at Health Canada linked known cases of hepatotoxicity to black cohosh-labeled "natural health products" (as they are termed in Canada) that contained Asian relatives of black cohosh, thereby more closely implicating the Asian adulterant(s) with some of the recent cases of hepatotoxicity associated with products labeled as containing black cohosh.


Black Cohosh *Actaea racemosa*. Photo ©2013 Steven Foster

Commercial Chinese websites offering "black cohosh extract" in tonnage at prices that vary by 300-fold list botanical source species for extract as an *Actaea* or *Cimicifuga* species, or sometimes as *Vernonia aspera* (*hei shengma*). Another member of the Asteraceae, *Serratula chinensis*, also may be sourced as *hei-shengma* (black cohosh), but is usually seen under the Chinese name *guang-dong shengma*. Analytical methods were not found for distinguishing these species in the supply chain.

To comply with appropriate current Good Manufacturing Practices (cGMPs) as required by law in the United States and many other countries requires only the will to do so and the subsequent access to appropriate quality control resources. Mislabeling or confusion may be due to simple language and translation variations, or, in some cases, the actual intent to sell a lower-cost material that is not an acceptable substitute for authentic North American black cohosh. However, these are possibly moot points as all of the identification and authentication scientific tools necessary to distinguish authentic black cohosh from any other plant materials of any origin are readily available.

Solving the problem of economic adulteration of black cohosh products is within reach. Many in the herb industry are acutely aware of the need for fulfillment of cGMPs as FDA increases cGMP inspections, compliance, and the issuance of 483s warning letters.[‖] Clearly, the crux of the problem of black cohosh adulteration lies squarely on the doorstep of intentional economic adulteration with less expensive materials from China. HG

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‖ The Director of FDA's Dietary Supplement Programs within the Center for Food Safety and Applied Nutrition, Daniel S. Fabricant, received his PhD in Pharmacognosy from the University of Illinois at Chicago under the tutelage of major and dissertation advisor the late Norman R. Farnsworth. Dr. Fabricant's dissertation was "Pharmacognostic Investigation of Black Cohosh (*Cimicifuga racemosa* (L.) Nutt.)".[91]

Black Cohosh *Actaea racemosa.* Photo ©2013 Steven Foster

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Black Cohosh *Actaea racemosa*. Photo ©2013 Steven Foster

Plant-Based Insect Repellents Provide an Alternative to Synthetic Formulas

By Tyler Smith

Catnip *Nepeta cataria*. Photo ©2013 Steven Foster

By the end of 2012, the US Centers for Disease Control and Prevention (CDC) had reported nearly 250 West Nile virus-related deaths in the United States. With more than 5,300 reported cases in 2012 — the most in nearly a decade[1] — health officials are urging individuals to take certain precautions to avoid being bitten by mosquitoes, which can carry the virus. In addition to ensuring properly fitting screens on windows and doors, wearing pants and long-sleeved clothing when outdoors, and avoiding pools of stagnant water where mosquitoes lay eggs, the CDC recommends using an insect repellent with an active ingredient registered by the Environmental Protection Agency (EPA).[2]

Of EPA-registered active ingredients, the most widely recognized and studied synthetic compound is DEET (*N,N*-Diethyl-3-methylbenzamide), an insect repellent developed by the US Department of Agriculture (USDA) in 1952 and approved for public use in the late 1950s.[3] Extensive testing supports the use of DEET as an effective method of preventing mosquito and tick bites, but mild skin and eye reactions have been reported, as well as several cases of seizures in individuals who frequently used DEET. EPA requires all DEET-containing products to contain detailed instructions for safe use, which includes avoiding over-application of the repellent and washing any treated skin or clothing after use. According to the EPA's 1998 reregistration eligibility decision, "DEET is not believed to be acutely toxic nor carcinogenic, significantly developmentally toxic nor mutagenic at the doses tested." Further, the EPA concluded that the "available data do not support a direct link between exposure to DEET and reported seizure incidences (14 cases)."[4]

In recent years, however, much research has been conducted on plant-based alternatives to synthetic formulas, which may be preferable to consumers with chemical sensitivities or those who wish to avoid synthetics.

"[Plant-based insect repellents] may be more cosmetically appealing, more widely available or producible, including in tropical countries where the public health value of repellents is especially important," said Scott P. Carroll, PhD, a scientist affiliated with the Department of Entomology at the University of California-Davis (email, September 25, 2012). "Plants are great biochemical synthesists, and we are well adapted to plants, so it's obviously functionally prosperous for investigation."

Appeal of Plant-Based Insect Repellents

Plants produce chemicals that act as natural deterrents to pests, and they have been used since ancient times to repel insects, most commonly by burning plant material.[5] The established use of plants as insect repellents in part contributes to their acceptability among consumers.

"There are quite a few natural products (oils and single compounds) that demonstrate repellent efficacy," said Ulrich R. Bernier, PhD, a research chemist in the Mosquito and Fly Research Unit at the USDA's Center for Medical, Agricultural, and Veterinary Entomology (email, September 21, 2012). "One advantage of using a plant-based botanical is user acceptability. People tend to favor natural products over synthetics."

Plant-based active ingredients also are thought by some to pose fewer risks to users. And since repellents are often applied directly to the skin, consumers tend to favor products without harsh chemical smells. Although, according to some experts, an effective active ingredient is the most important consideration when choosing an insect repellent, personal preference plays a role in repellent selection as well.

"There is a strong perception that natural actives are safer than synthetics," said Sarah J. Moore, PhD, a lecturer in the Department of Disease Control at the London School of Hygiene and Tropical Medicine, and a co-author of a 2011 review of plant-based insect repellents published in *Malaria Journal* (email, September 21, 2012). "Plant-based odours are scents that people feel comfortable with as they are natu-

Catnip *Nepeta cataria*. Photo ©2013 Steven Foster

Catnip *Nepeta cataria*. Photo ©2013 Steven Foster

ral. My research on [multiple] continents (North and South America, South-east Asia and Africa) has highlighted this same perception."

Perhaps more importantly, insect repellents derived from plants can be an inexpensive, sustainable method of preventing disease in high-risk regions of the world. "If plant-based repellents are ethically sourced and produced then they can bring trade [to] developing countries and are less damaging to the environment," said Dr. Moore.

In 1996, the EPA began compiling annual lists of newly approved biopesticide active ingredients.[6] Biopesticides are defined as "naturally occurring substances that control pests (biochemical pesticides), microorganisms that control pests (microbial pesticides), and pesticidal substances produced by plants containing added genetic material (plant-incorporated protectants) or PIPs."[7]

However, before being marketed, the Federal Insecticide, Fungicide, and Rodenticide Act requires the EPA to conduct rigorous testing of the ingredient to ensure that it does not pose a risk to human health or the environment.[7]

The first year records were available, six ingredients were addressed, including a German cockroach pheromone and multiple bacteria-derived ingredients. In 2010, the most recent year for which records are available, the list included 17 approved active ingredients, almost three times as many as were first approved in 1996. Combined, the annual lists contain more than 100 approved biopesticide active ingredients; however, only a small fraction of this number are specifically plant-based insect repellents.

Hydrogenated Catmint (Catnip) Oil

In December 2008, the EPA approved hydrogenated catmint oil (*Nepeta cataria*, Lamiaceae), a species of the mint family. Catmint, or catnip as it is more commonly referred to*, is best known for its ability to produce behavioral changes when given to cats, which typically last only a few minutes. The chemical believed to be responsible for this intoxication-like behavior in cats is known as nepetalactone, a mild hallucinogen.[8]

"[Catmint oil] is in the pipeline for becoming available as a consumer product, and [has] better lasting properties than citronella," said Dr. Carroll (email, October 1, 2012).

According to the American Mosquito Control Association (AMCA), "Catnip has been noted for years as possessing repellency against mosquitoes. However, only recently has its efficacy been demonstrated to the extent it could be registered by the EPA."[9]

The EPA has registered four formulations of catmint oil, including liquids and lotions with various percentages of the active ingredient. Each of these products is currently made by DuPont and exhibit protection times between seven and 15 hours.[10] AMCA points out that "A commercial version is not yet available, though. Catnip products currently available through internet suppliers do not possess an EPA registration that validates its efficacy."[9]

In 2007, Spero *et al*. published the results of repellency activity of hydrogenated catmint oil against mosquitoes and black flies in the *Journal of Medical Entomology*. According to the authors, "Iridoid monoterpenoids such as nepetalactone have long been known to be repellent to some insect species.… The related compound dihydronepetalactone (DHN) is also an effective repellent of a number of biting insect species."[11]

Although DHN comprises only a small percentage of the oils of *N. cataria,* the authors explained that it can be produced by a chemical process known as catalytic hydrogenation of the nepetalactones in the oil, hence the name "hydrogenated" catmint oil.[11]

Spero *et al*. reported that hydrogenated catmint oil (HCO) offered protection for more than four hours, with a 15% lotion providing protection of more than eight hours. They concluded that their results "indicate strongly that HCO in different topical formulations offers an effective alternative to existing natural and synthetic insect repellents."[11]

In the following year, Polsomboon *et al*. examined two separate categories of behavioral responses of mosquitoes to catmint oil — contact irritancy and non-contact repellency — in a paper published in the *Journal of the American Mosquito Control Association*. Using two species of mosquitoes, the researches determined that "catnip oil has strong irritant and repellent actions on mosquito test populations as indicated by the comparatively low escape time."[12]

In its fact sheet on HCO, the EPA cited that "no risks to human health will be expected from the use of Hydrogenated Catmint Oil based on its low toxicity and current use as a food ingredient by the general public without any reported adverse effects on human health." Further, in the environmental risk section of the fact sheet, they concluded that "it is not likely to accumulate in drinking water," nor is it "expected to occur or pose a threat to non-target organisms."[13]

Repellents Derived from the Lemon Eucalyptus Tree

In April 2005, the CDC approved botanically based paramenthane-3,8-diol, or PMD, as an effective insect repellent.[14] PMD, which is derived from leaves of the lemon eucalyptus tree (*Corymbia citriodora,* Myrtaceae), was discovered in the 1960s by researchers conducting chemical screenings for potential insect-repelling properties of plants used in Traditional Chinese Medicine. In fact, as plants are occasionally named in accordance with their traditional uses, the Chinese name for lemon eucalyptus, *quwenling*, translates roughly to "effective mosquito repeller."[15]

Although there are multiple plant-based active ingredients registered with the EPA, researchers have reported that PMD is "the only plant-based repellent that has been advocated for use in disease endemic areas by the CDC, due to its proven clinical efficacy to prevent malaria and is considered to pose no risk to human health. [PMD] provides very high protection from a broad range of insect vectors over several hours."[5]

PMD is not to be confused with what is frequently referred to as "oil of lemon eucalyptus." In distilling the essential oil from leaves of the lemon eucalyptus tree, PMD is left over as a waste product.[5] It is this waste product that has been shown to be effective in repelling mosquitoes, more so than the oil itself. Although insect repellent products containing oil of lemon eucalyptus are available, Dr. Moore cautions against using anything but CDC- and EPA-recommended active ingredients, such as PMD, in areas with disease risk.

Depending on the concentration, PMD formulas can last up to eight hours,[15] and have been shown to be almost as effective as those containing DEET. In some cases, PMD has been shown to be *more effective* than DEET in repelling certain species of mosquitoes.

"[Some plant-based ingredients can] better repel certain vectors, as in the case of PMD's evident superiority to DEET in repelling *Anopheles* malaria vectors," said Dr. Carroll. In a 2006 study published in the *Journal of the American Mosquito Control Association,* of which Dr. Carroll was a co-author, he wrote that "PMD has shown unprecedented repellency and consistency for a botanical."[15]

Similarly, Dr. Moore, who conducts field research around the world, has found that PMD is consistently effective. Although her research primarily concerns the prevention of malaria, the same mosquito-repelling properties will protect against other mosquito-borne diseases such as West Nile fever and encephalitis, dengue fever, and yellow fever.[16]

"I can attest to the fact that PMD repellents are highly effective from both my research where they demonstrate good efficacy and the research of others who all show a consistently good effect in preventing bites from disease-vector insects," she said. "I have lived in Tanzania for the past 6 years in a highly malarious area where we use PMD every evening in conjunction with long clothing, and we screen our home and use an insecticide-treated bed net as recommended best practise. I have never had a negative skin reaction or a vector-borne disease. Malaria is a preventable disease and we have effective tools, both synthetic and natural, to combat it."

Lemon Eucalyptus Tree *Corymbia citriodora*
Photo ©2013 Steven Foster

Citronella-Based Insect Repellents

Although PMD is a widely studied natural insect repellent, the plant-based ingredient citronella is arguably more recognized as a mosquito repellent. Citronella oil has been shown to be less effective than DEET, but it still can be a useful tool for repelling mosquitoes in areas without disease risk.

"Citronella has found its way into many commercial preparations through its familiarity, rather than its efficacy," said Dr. Moore. "Citronella-based repellents only protect from host-seeking mosquitoes for about 2 hours."

Citronella was first registered by the EPA in 1948 and was originally used in perfumes for its pleasant scent.[4] Today, citronella candles are ubiquitous in American backyards, although it also is used in creams, lotions, and sprays. According to the EPA, citronella is classified as a biopesticide and registered as an insect repellent or feeding

Citronella *Cymbopogon nardus*
Photo ©2013 Steven Foster

depressant and also as an animal repellent. Oil of citronella comes from 2 species of aromatic grasses, Ceylon citronella (*Cymbopogon nardus*, Poaceae) and Java citronella (*C. winterianus*). Citronella is regarded as a highly safe repellent; in a 1997 reregistration memo, the EPA concluded that "based on available data, the use of currently registered products containing oil of citronella in accordance with their approved labeling will not pose unreasonable risks or adverse effects to humans or the environment."[17]

Hydrogenated catmint oil, citronella, and PMD are just three of the hundreds of plants or plant-based ingredients that have been studied for their insect-repelling properties. In addition to hydrogenated catmint oil, citronella, PMD, and DEET, Health Canada — the governmental body responsible for national public health in Canada — has approved products containing soybean (*Glycine max*, Fabaceae) oil for mosquito-repelling purposes for up to 3.5 hours, although less research has been conducted on this particular ingredient. Other commonly-cited botanicals used to repel mosquitoes include species in the mint family (basil [*Ocimum basilicum*] and peppermint [*Mentha* x *piperita*]), 2-undecanone (an extract from tomato plants [*Solanum lycopersicum,* Solanaceae]), neem oil (*Azadirachta indica,* Meliaceae), lemongrass (*Cymbopogon citratus,* Poaceae), fennel (*Foeniculum vulgare,* Apiaceae), and rue (*Ruta graveolens,* Rutaceae).[18-20]

Issues Associated with Plant-Based Repellents

As a scientific term, volatility refers to a chemical's tendency to evaporate. Bruised or damaged plants will release volatile odors into the environment, which can offer protection from pests at a distance.[4] However, when these chemicals are formulated into insect repellents that are applied to the skin, volatility becomes a problem.

PMD is unique in that it has an especially low vapor pressure, which causes it to evaporate slower than other plant-based insect repellents. Citronella, however, upon initial application, is just as effective as DEET, but its high volatility quickly decreases its effectiveness.

"Some plant-based molecules are incredibly effective in the short term but quickly evaporate and for this reason they don't last as long as the synthetic molecules," explained Dr. Moore.

According to Dr. Bernier, volatility is one of the challenges to formulating an effective and long-lasting botanical insect repellent. "One the greatest problems with naturally based repellents is the volatility of those oils or compounds within oils that contribute to the observed repellency," he said. "There are a number of natural compound repellents on the market and some of these do repel for a short time."

However, there are some ways to mitigate the effects of the high volatility of plant-based active ingredients. One option is to combine plant-based chemicals with larger molecules that evaporate more slowly. Vanillan, a relatively large molecular component of the vanilla bean (*Vanilla* spp., Orchidaceae), has been added with some success to botanical insect repellent formulas to reduce the formulas' volatility.[5] And in recent years, advances in nanotechnology have provided even more options to increase the duration of plant-based repellents. These techniques have been used in some citronella formulas. For example, "[e]ncapsulated citronella oil nanoemulsion [can be] prepared by high-pressure homogenization … to create stable droplets that increase the retention of the oil and slow down release."[5]

To counteract the high volatility of some plant-based active ingredients, some mosquito repellents contain higher concentrations of these ingredients. And as with any dermatological applications of chemicals — plant-based or synthetic — there is some risk of a reaction.

"Some essential oils can cause skin irritation," said Dr. Moore. "Read the label — if there are high concentrations of essential oils they are unlikely to be suitable for those with sensitive skin. If you have a reaction, immediately discontinue use and consult a physician if you have a dermatitis that does not resolve after a few days."

As consumer interest in plant-based products grows, scientists will continue to study plants to learn more about their insect-repelling properties. Botanical formulas, when used properly, provide an alternative to synthetic repellents. Although plant-based insect repellents often are not as effective as DEET, in time, this may change.

"As technology improves so that formulations make essential oils and other plant based molecules remain on the skin for as long as DEET, then we will see more effective plant-based repellents that can be used to prevent disease. I am certainly keen to see this happen if it means that products can be made in a more environmentally sustainable way through fair trade," said Dr. Moore. "It will hopefully help make repellents such as citronella and PMD more accessible to those living in disease endemic countries of the tropics because they often cannot afford to purchase repellents imported from outside. I am keen to see more manufacturers taking on this challenge."

**Catnip is the Standardized Common Name (SCN) according to the American Herbal Products Association's* Herbs of Commerce, *2nd edition. Catmint is the Other Common Name (OCN).*

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Chase Tree Berry *Vitex agnus-castus.*
Photo ©2013 Steven Foster

Treating PCOS Naturally

Clinical experience and scientific evidence support medicinal herbs, nutritional supplements, and lifestyle interventions to treat symptoms of this common female endocrine disorder

By Lindsay Stafford Mader

Polycystic ovarian syndrome (PCOS) — a hormonal endocrine disorder that affects more than 5 million women in the United States alone — manifests itself through a spectrum of symptoms, including irregular or absent menstruation (known as amenorrhea), lack of ovulation, multiple cysts on the ovaries, acne, excessive facial hair (hirsutism), and obesity.[1] (Many women with PCOS are of normal weight — referred to as "lean" PCOS.) PCOS is one of the leading reasons behind female infertility, and it also increases the likelihood of miscarriage and infant death during or shortly after birth. Additionally, PCOS can lead to serious health issues, including endometrial cancer, osteoporosis, heart disease, and diabetes.[1]

While the cause of PCOS is uncertain, complex, and variable, several conditions are present within the bodies of women with PCOS that lead to their often-distressing symptoms. These typically include higher-than-normal levels of male hormones — particularly testosterone — lower-than-normal levels of the female hormone progesterone, elevated levels of the hormone prolactin in some cases, and abnormal insulin regulation.[1]

Drugs prescribed for PCOS include oral contraceptives, which decrease male hormone levels and may normalize a woman's menstrual cycle, and metformin (brand name Glucophage®), a drug commonly used to treat type 2 diabetes that has been found to help PCOS patients regulate insulin levels and support conception.[1] Women with PCOS who are trying to conceive are sometimes prescribed clomiphene (Clomid,™ Serophene®), a fertility drug that stimulates ovulation.

These pharmaceuticals, unfortunately, are not without significant drawbacks. Oral contraceptive pills often produce myriad side effects (increased appetite, mood swings, weight gain, nausea, etc.), cannot be used by women with PCOS who are trying to conceive, and frequently worsen insulin resistance in PCOS patients.[2] Clomid can lead to undesired multiple-birth pregnancies,[2] and the US Food and Drug Administration (FDA) warns that it increases the risk of major birth defects and should not be used in pregnancy.[3] Although metformin is showing potential to help manage PCOS symptoms and perhaps boost conception chances, some women experience discouraging gastrointestinal side effects from the drug,[4] which has not been approved by FDA to treat PCOS.[1]

"Herbs are important as there are few truly effective pharmaceutical options," said Jillian Stansbury, ND, a Washington state-based naturopathic physician and author of *The PCOS Health and Nutrition Guide* (Robert Rose, 2012). "Herbs are a safe and nutritive option to support ovarian function, endocrine feedback loops, thyroid function, and blood sugar regulation and metabolism. I have had a great many patients with PCOS over the years, and can report overall good success in treating the various forms and presentations of PCOS: helping women lose weight, restoring normal menses, helping infertile women to conceive and carry the pregnancy, and improve metabolic function and prevent diabetes" (email, February 11, 2013).

Integrative medicine physician, herbalist, and midwife Aviva Romm, MD, agrees that herbs play a significant role

in PCOS treatment. "Weight loss is the most effective intervention, and metformin is actually not a bad option, but of course herbs are natural and generally safe so a great option to at least try for folks wanting to avoid pharmaceuticals," said Dr. Romm (email, February 10, 2013). "They might be particularly helpful in the insulin resistance aspects of the condition, as well as stress hormone mediation."

The PCOS section in Dr. Romm's 2010 book, *Botanical Medicine for Women's Health* (Churchill Livingstone), illustrates the potential that herbs offer for this complex condition by presenting a successful case report. Author of the section, Angela Hywood, ND, writes that the PCOS patient took six herbs* — chaste tree berry (*Vitex agnus-castus*, Lamiaceae), licorice (*Glycyrrhiza glabra*, Fabaceae), white peony (*Paeonia lactiflora*, Paeoniaceae), gymnema (*Gymnema sylvestre*, Apocynaceae), echinacea (*Echinacea* spp., Asteraceae), and schisandra (*Schisandra chinensis*, Schisandraceae) — in addition to eating a low-carbohydrate diet. According to the report:

> After five months on the herbal protocol, the patient's cycle regulated to a 32-day length…. Problematic symptoms such as mastalgia [breast pain], acne, and hirsutism diminished significantly during the five-month program. The lipid profile has improved to within normal ranges…. She lost a total of 12 percent body weight in the five months. The client became pregnant in her second month of actively trying to conceive.[2]

Natural treatment plans formulated for PCOS patients by NDs, herbalists, and integrative physicians typically focus on addressing three main types of PCOS manifestations: (1) hormonal imbalances; (2) insulin, blood sugar, and metabolic sensitivities and/or irregularities; and (3) stress response and management.

"My general approach has emphasized diet and exercise as a foundational therapy," said Dr. Stansbury, "and I create specific herbal and nutritional protocols for individual patients. Because PCOS has many presentations, there could be a variety of different approaches to address specific presentations."

The following herbs and other natural approaches for treating PCOS and its symptoms are based on practitioners' experience in treating women with PCOS, as well as several controlled human studies. The numerous medicinal plants, substances, and techniques discussed herein represent a broad overview of this mixed-source data, and are not being suggested for comprehensive or concurrent use.

Balancing Hormones

Because PCOS is an endocrine disorder, herbs that balance hormone levels can be very helpful in improving most PCOS symptoms, including amenorrhea, infertility, acne, and excessive facial hair. Women who have been diagnosed with PCOS or those who think they might have PCOS should obtain a blood test in order to determine if their testosterone and/or prolactin levels are increased. If they are, Dr. Stansbury suggests chaste tree berry, licorice root, and the Traditional Chinese Medicine (TCM) herb *dong quai* (*Angelica sinensis*, Apiaceae) root to restore normal menses. (For herb use during pregnancy, please see the "Conclusion" section on page 63.)

"I have seen many amenorrheic women be able to regain their menses — some of them quite quickly," said Dr. Stansbury. "I remember one case with a woman who hadn't had a menses for more than three years begin to menstruate after two weeks on an herbal tincture of chaste tree, saw palmetto, and licorice. And then we did some trial-and-error, and when we stopped the formula, her menses would stop again."[5]

Because PCOS is an endocrine disorder, herbs that balance hormone levels can be very helpful in improving most PCOS symptoms, including amenorrhea, infertility, acne, and excessive facial hair.

Chaste tree has been used for thousands of years for numerous women's health issues, including menstrual disorders. Although no existing studies have directly examined its effects in PCOS patients, a small collection of published scientific and clinical evidence supports its ability to treat some of the condition's symptoms.[6] Several older clinical trials reportedly found chaste tree to result in normal menstrual cycles,[6] and more recent research has shown that it is successful at decreasing elevated prolactin levels and improving fertility and the body's progesterone-producing process.[7]

Licorice, a well-researched medicinal plant in the legume family, contains compounds that exhibit estrogenic activity. Some studies have found licorice to reduce testosterone levels in healthy women, suggesting that it might also be useful for women with PCOS.[8] Dong quai also exhibits estrogenic activity, and has been used for many years to treat gynecological conditions. While more research is warranted to support its traditional uses, limited evidence has found that it can successfully treat amenorrhea.[9]

For women whose PCOS-related hormone imbalances are making conception difficult, Dr. Stansbury recommends several herbs, including chaste tree berry, dong quai, Indian kudzu (*Pueraria* spp., Fabaceae) leaf, and knotweed (*Polygonum multiflorum*, Polygonaceae) root. Although these herbs have been shown in her clinical practice to help women with PCOS to conceive, Dr. Stansbury notes that success varies and can take longer when working toward this more complex outcome, and thus several herbal combinations are often formulated and tried on each individual patient. In her 1999 book *Women's Encyclopedia of Natural Medicine* (Keats Publishing), Tori Hudson, ND, suggests that chaste tree be taken for at least three or four months.[6]

Additional menstruation-normalizing/hormonal-balanc-

Red Clover *Trifolium pratense.* Photo ©2013 Steven Foster

ing herbs recommended by various naturopathic doctors and herbalists based on their clinical experience and traditional history include the following:

- red raspberry (*Rubus idaeus*, Rosaceae) leaf
- saw palmetto (*Serenoa repens*, Arecaceae) berry
- ginger (*Zingiber officinale*, Zingiberaceae) root/rhizome
- rosemary (*Rosmarinus officinalis*, Lamiaceae) herb
- feverfew (*Tanacetum parthenium*, Asteraceae) leaf
- partridge berry (*Mitchella repens*, Rubiaceae)*
- mugwort (*Artemisia vulgaris*, Asteraceae) herb
- false unicorn (*Chamaelirium luteum*, Melanthiaceae) root — a North American herb with an at-risk conservation status.

The following phyto-estrogenic herbs also are recommended:

- black cohosh (*Actaea racemosa*, Ranunculaceae) root/rhizome
- red clover (*Trifolium pratense*, Fabaceae) flower
- alfalfa (*Medicago sativa*, Fabaceae) herb
- flax (*Linum usitatissimum*, Linaceae) seed
- soy (*Glycine max*, Fabaceae) bean, and
- hops (*Humulus lupulus*, Cannabaceae) strobiles.[2,5,6,10,11]

Although little human clinical research has been conducted on herbs specifically for PCOS treatment, some new studies present promising possibilities. A traditional Japanese formulation of licorice and white peony — called *Shakuyaku-Kanzo-To* — has been shown in trials on women with and without PCOS to decrease testosterone levels, stimulate ovulation, and promote conception.[2]

A 2013 Iranian study on dried aerial parts of wood betony (*Stachys lavandulifolia*, Lamiaceae) found that this mint-family herb ameliorated abnormal uterine bleeding in PCOS patients as well as the synthetic progesterone, and that it lowered testosterone levels and improved ovarian condition more than the progesterone.[12]

Similarly, a study on the black cohosh root extract Klimadynon® (an ethanolic extract produced by German company Bionorica) found that it increased PCOS patients' progesterone levels, significantly reduced luteinizing hormone levels, and improved ovulation and endometrial thickness more than Clomid.[13] Although pregnancy rates were higher in the black cohosh group, the difference was not statistically significant.

A 2010 controlled trial on 80 women with PCOS found that a maitake mushroom (*Grifola frondosa*, Polyporaceae) extract significantly increased ovulation when used alone and in combination with clomiphene.[14] While subjects taking the maitake had approximately 77 percent ovulation — which Dr. Hudson noted as "quite impressive" — clomiphene rates of ovulation were higher at 93.5 percent.[15]

Improving Insulin Regulation

Many women with PCOS have insulin resistance, also known as metabolic syndrome, which presents itself through weight gain, high blood pressure, high blood sugar, and high cholesterol. Others experience insulin resistance-related hyperinsulinemia, which is higher-than-normal levels of insulin in the blood that can cause hyperglycemia as well as hypoglycemia (low blood sugar), the latter of which produces symptoms such as lightheadedness, nausea, shaking hands, and confusion. A woman who has been diagnosed with PCOS or who thinks she might have the condition should have her blood tested for insulin sensitivity. If she is found to exhibit full or partial manifestations, the pharmaceutical metformin usually is prescribed, and several herbs and foods exhibit similar therapeutic actions. Due to their inositols and related compounds, Dr. Stansbury noted that legumes are especially good for women with PCOS-related insulin concerns.

"These compounds work together to treat insulin resistance," she said. "They support signal transduction, the ability of a cell to receive insulin and then tell the nucleus of the cell to respond to it."

Not only have inositols garnered positive clinical outcomes among herbalists and NDs, but their use in treating PCOS also has been supported by clinical trials.

Not only have inositols garnered positive clinical outcomes among herbalists and NDs, but their use in treating PCOS also has been supported by clinical trials. A randomized, controlled clinical trial published in a 2010 issue of the journal *Gynecological Endocrinology* found that a daily dosage of 4 grams myo-inositol and 400 mcg folic acid significantly increased ovulation and conception rates in infertile PCOS women compared with 1,500 mg daily of metformin.[16] Another inositol form — D-chiro-inositol — also has been shown in earlier human studies to be very effective at treating PCOS,[17] and more recent research suggests a combination of the two forms may be just as effective.[18,19] Studies are currently comparing the two against each other.[20] (Furthermore, a small, controlled, randomized clinical trial has shown myo-inositol to be superior to D-chiro-inositol in improving embryo quality and pregnancy rates.[21]) Good sources of inositols are brown rice (*Oryza sativa*, Poaceae); legume family (Fabaceae) plants including soy, kidney beans (*Phaseolus vulgaris*), garbanzo beans (*Cicer arietinum*), carob (*Ceratonia siliqua*) — available in powder form or in supplements — astragalus (*Astragalus membranaceus*), and alfalfa; and legume-family herbs such as licorice. Small amounts of D-chiro-inositol are found in buckwheat (*Fagopyrum esculentum*, Polygonaceae). Inositol supplements also are available over-the-counter at many health food stores.

Dr. Stansbury recommends eating as much beans as possible. "As much one can stand, thus a cup or more daily," she said. "Lentils, split pea soup, hummus, baked beans, black bean soup, kidney beans in salads, refried beans.... There are unlimited possibilities." She additionally recommends prickly pear (*Opuntia ficus-indica*, Cactaceae) fruit for improving insulin resistance,[5] an action that has been supported by years of use in traditional Mexican medicine as well as in preliminary animal and human studies, which found the fruit to lower high blood sugar.[22] Additional *in vitro* and animal studies found prickly pear to lower triglyceride, low-density lipoprotein cholesterol, and total cholesterol levels — all of which can be a concern for women with PCOS. Dr. Stansbury suggests using several tablespoons of prickly pear fruit juice in smoothies or sparkling water, or using a splash with vinegar and oil for salad dressing or as a marinating sauce.[5]

Vitamin D, which enhances the action of insulin, also can be helpful, as well as the mineral chromium.[5] According to the PCOS section in the 2010 book *Integrative Women's Health*, "accumulating evidence" supports chromium for enhancement of "the metabolic action of insulin and decreasing total cholesterol and LDL…. It has the greatest benefit on obese, insulin-resistant individuals."[4] Integrative medicine physician and author of this section, Bridget Bongaard, MD, recommends 200 to 1,000 mcg of chromium picolinate per day,[4] and the mineral also can be found in brewer's yeast, hibiscus (*Hibiscus sabdariffa*, Malvaceae) flowers and calyx, dandelion (*Taraxacum officinale*, Asteraceae) leaves, stevia (*Stevia rebaudiana*, Asteraceae), and lemongrass (*Cymbopogon citratus*, Poaceae).[5]

Dr. Bongaard additionally advises PCOS patients to consider ingesting moderate amounts of tea (*Camellia sinensis*, Theaceae) and/or coffee (*Coffea arabica*, Rubiaceae) due to caffeine's well-documented ability to improve insulin sensitivity, taking 1 to 6 grams daily of cinnamon (*Cinnamomum verum*, Lauraceae) for its ability to improve insulin resistance and reduce fasting blood glucose — activities exhibited in human trials — or 200 to 400 mg of alpha-lipoic acid to reduce insulin resistance and oxidative stress.[4] Dr. Hywood writes in *Botanical Medicine for Women's Health* that the traditional anti-diabetic Indian herb gymnema has been shown in experimental models to lower blood sugar levels by preventing glucose absorption, and that fish oil may also benefit PCOS patients due to its reduction of serum triglycerides.[2]

Stress Response and Management

An important yet perhaps less-recognized aspect of PCOS treatment is managing a patient's stress level. As Dr. Hywood explains, "In response to stress, the adrenals release cortisol, inducing an elevation in prolactin … and increased androgen synthesis, which in turn leads to menstrual cycle dysregulation, especially anovulation, characteristic of PCOS." In fact, Dr. Hywood notes that botanical PCOS treatments should first address stress and that adaptogenic herbs "should be given primary consideration" because they "improve resistance to stress through [modulation] at the adrenal level." She lists the following herbs as helpful adaptogens for PCOS treatment (plant parts not specified):

- ashwagandha (*Withania somnifera*, Solanaceae)
- American ginseng (*Panax quinquefolium*, Araliaceae) and Asian ginseng (*P. ginseng*)
- licorice
- rhaponticum (*Rhaponticum carthamoides*, Asteraceae)
- rhodiola (*Rhodiola rosea*, Crassulaceae)
- schisandra

In *Integrative Women's Health*, Dr. Bongaard recommends various mind-body therapies, including yoga, guided visualization, hypnosis, biofeedback, and aromatherapy for decreasing stress hormones and improving blood pressure and blood sugar. In fact, a recent controlled study conducted in India and published in the July 2012 issue of the *International Journal of Yoga* found that a daily, hour-long yoga and meditation program improved anxiety symptoms in teenage girls with PCOS.[23]

Conclusion

Additional supportive therapies for PCOS include nurturing a healthy liver — an organ crucial to the breaking down

Red Raspberry Leaf *Rubus idaeus.* Photo ©2013 Steven Foster

Prickly Pear Fruit *Opuntia ficus-indica.* Photo ©2013 Steven Foster

of excess hormones — particularly through limiting alcohol intake and ingesting liver-supportive herbs such as milk thistle (*Silybum marianum*, Asteraceae).[5] Dr. Stansbury highlighted the significant role that alcohol plays in women with PCOS, for whom she recommends limiting consumption to just a few alcoholic drinks per week, if any at all.

"Alcohol has one of the biggest glycemic indices of any foodstuff, more than eating a spoonful of sugar.[5] So if anyone is prone to insulin resistance, quantities of alcohol will just challenge your blood sugar regulation. Alcohol also challenges the liver, of course, and if your liver is busy detoxifying alcohol, then it has less enzymes or less power and reserves to metabolize your hormones."

Regular and moderate exercise and resultant weight loss is paramount for overweight PCOS patients as it reduces insulin and testosterone levels — often providing dramatic relief of most PCOS symptoms.[2,4] "Weight loss alone," writes Dr. Hywood, "has led to achievement of pregnancy in 60% of cases without other medical intervention." Likewise, low-carb, whole foods diets also have been shown in clinical experience and human studies to reduce insulin resistance and testosterone levels in women with PCOS.[5,24] Additionally, a small controlled clinical trial recently found that acupuncture increased the frequency of ovulation in women with PCOS.[25]

Although women with PCOS are understandably eager to improve their symptoms, enjoy an improved quality of life, and, often times, to start a family, they must keep in mind that herbal, nutritional, and lifestyle therapies can take time. In fact, Dr. Stansbury recommends that PCOS women hoping to have children "take several months, even a year, to prepare yourself, improve your fertility, and decrease the chance of miscarriage by improving your diet and by taking key supplements."[5]

"[Women] might notice improvement as early as a month or two," said Dr. Stansbury, "but since this is shifting your whole hormonal balance and acting on the liver and adrenals and ovarian function and pituitary feedback loops, I give women a six-month to 12-month game plan."

If a woman with PCOS conceives a child, most of the herbs mentioned above should not be used during pregnancy, unless recommended by the patient's healthcare provider.[2] A few — including ginger, red raspberry leaf, echinacea, and partridge berry — have safe pregnancy profiles.[10] As in most cases, readers are advised to consult their healthcare provider for more information. HG

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Carob *Ceratonia siliqua.* Photo ©2013 Steven Foster

Historic photo of Schwabe Pharmaceuticals analytical laboratory.
Photo ©2013 Schwabe

Dr. Willmar Schwabe Pharmaceuticals:
An Herbal Legacy Company

German Namesake's Founding Values Continue to Guide Company Practices

By Tyler Smith

Editor's note: This is the second article in a series on legacy herbal businesses that have been operating for more than 100 years.

In 1866, just three years after receiving his doctorate in pharmaceutics, Willmar Schwabe founded the company that still bears his name. At the time, the world was experiencing significant scientific advancements, including the use of early anesthetics such as ether and chloroform, and the development of aspirin, based on a synthetic chemical modeled after salicin, originally derived from the bark of the white willow tree (*Salix alba*, Saliaceae).[1,2] Almost a century and a half later, Dr. Willmar Schwabe Pharmaceuticals has become an industry leader in natural pharmaceutical research and development, and is generally acknowledged as the leading manufacturer of phytomedicines worldwide.[3]

A little over a decade after Dr. Willmar Schwabe Pharmaceuticals was founded, the company launched its first phytomedicinal product, Schwabe's hamamelis ointment, a witch hazel (*Hamamelis virginiana*, Hamamelidaceae)-based hemorrhoid cream. In 1917, Dr. Schwabe's son, Willmar Schwabe II, inherited the company. Today, Schwabe Pharmaceuticals maintains its status as an independent, family-owned business and is currently in its fifth generation.[3]

"Schwabe always has been a family-owned company," said Uta Hülsermann, PhD, Schwabe's official spokesperson (email, January 10, 2013). "There have been three Willmar Schwabes over the generations."

One of the original Willmar Schwabe's most significant contributions to herbal medicine was the 1872 publication of *Pharmacopoeia Homeopathica Polyglotta*, a homeopathic pharmaceutical reference guide that has largely withstood the test of time. "Dr. Willmar Schwabe's *Pharmacopoeia Homeopathica Polyglotta* received a lot of attention in its time because up to then, [there] existed a multitude of different Pharmacopoeiae and this publication was regarded as standard publication that finally 'cleared the mess,'" said Dr. Hülsermann (email, February 6, 2013). By 1872, it had been published in English, German, and French, and it remains an indispensable reference in all German pharmacies, she added.

Today, the company has expanded far beyond its original roots in Leipzig, Germany. Dr. Willmar Schwabe Pharmaceuticals, now headquartered in Karlsruhe, Germany, has more than 20 subsidiaries and joint ventures around the world, employing more than 3,500 people on five continents and in more than 60 countries.[4] Schwabe North America, which operates in the United States and Canada, comprises the well-known brands Nature's Way®, Enzymatic Therapy®, and Integrative Therapeutics®.[4]

Michael Devereux, chief executive officer of Schwabe North America, said it was Schwabe's commitment to improving the lives of individuals through natural products that led him to the company.

"What truly attracted me, though, was the mission of the business, and frankly of the industry, which is to focus on products and solutions tied into people improving their health and wellness," said Devereux (email, February 14, 2013). "Natural products that have existed from decades of studies on ingredients for safety and efficacy seems to me to be a great way to start on the path to improving your health, before introducing something that is not natural. They are a first-line solution."

Schwabe's first phytopharmaceutical product, "Schwabe's Hamamelis ointment," today's Hametum®. Image ©2013 Schwabe

A History of Evidence-Based Natural Medicine

The success of Schwabe's global operations stems from a commitment to values put forth by Dr. Willmar Schwabe: reliability, innovation, quality, and responsibility.[3]

"He already was dedicated to prove scientifically the efficacy of the plant extracts and to set quality standards for the extraction and production process," Dr. Hülsermann explained. "As a global leader in natural health, Schwabe strives to enhance the quality of life through innovative, safe, and efficacious products."

Schwabe's products are tested extensively for efficacy and safety in scientific studies and clinical trials. In total, Schwabe holds more than 800 registrations worldwide for its phytomedicines, most of which focus on four key therapeutic areas, including the central nervous and cardiovascular systems, as well as urological and respiratory conditions. The company's research division is responsible for numerous processes, from screening new plants for potential medicinal activity to conducting clinical trials of finished products.[3]

"Schwabe's clinical research on phytomedicines … has significantly contributed to the acceptance of science-based phytotherapy in the medical community," the company states on its website. "Looking back on the long in-house tradition of such studies, Schwabe Pharmaceuticals may be regarded as the inventor of evidence-based phytomedicine. Our dedication to proving the efficacy and safety of our phytomedicines through rigid pharmacological and clinical studies is unique."

In 2008, Schwabe was awarded the American Botanical Council's inaugural Varro E. Tyler Commercial Investment in Phytomedicinal Research Award. According to an HerbalEGram article about the award, "Many of the scientific methods and techniques developed and used by Schwabe during the past century have had a significant influence on today's pharmaceutical and biochemical research."

Top photo: Ginkgo plantation
Middle photo: Entrance of Schwabe headquarters in Karlsruhe, Germany. Photos ©2013 Schwabe

One of the scientific methods Dr. Willmar Schwabe developed for quality control was capillary analysis, a technique used to separate the components of a substance into its various phases using special absorbent paper. "Nowadays, this technique is obsolete, but was the basis for modern techniques, as for example, capillary electrophoresis or gas chromatography," said Dr. Hülsermann (email, March 28, 2013). "Those techniques are widely used in research, development, quality control and all other fields of analytics. Gas chromatography is used in our company as well."

Of all of Schwabe's products, the most-recognized is formulated from the ancient *Ginkgo biloba* (Ginkgoaceae) tree. "The most important and most popular product of Schwabe is EGb 761®, a special *Ginkgo biloba* extract," said Dr. Hülsermann. "EGb 761® is marketed worldwide in more than 60 countries. Depending on the market, it is used in the therapy of cognitive disorders such as dementia and cognitive impairment, vertigo and tinnitus, and PAOD (peripheral arterial occlusive disease)."

Other key Schwabe products include Prostagutt®, a saw palmetto [*Serenoa repens*, Arecaceae] berry extract product used in benign prostate hyperplasia therapy; Prostagutt® forte, a combination of saw palmetto extract and nettle (*Urtica dioica*, Urticaceae) root extract; Venoplant®, a horse chestnut [*Aesculus hippocastanum*, Sapindaceae] seed extract used in chronic venous insufficiency; and the latest development, Lasea®, a lavender [*Lavandula angustifolia*, Lamiaceae] flower essential oil-based product for subsyndromal anxiety disorder.

The importance of phytomedicines for consumers is a driving factor for Schwabe's continued research and development of new plant-based medicines. "In many cases, phytomedicines offer an additional therapeutic alternative in the treatment of patients," said Dr. Hülsermann. "With phytomedication, compliance is often better since [adverse] side-effects and drug-to-drug interactions occur in [fewer] cases and are generally less serious than with synthetic [pharmaceutical] agents."

Commitment to Quality and Sustainability

In addition to its focus on research, Schwabe controls virtually every other aspect of the development of its phytomedicines, from raw material production to pharmaceutical-grade manufacturing, as well as marketing and sales.[4]

"Schwabe 'owns' the production process of many of its phytomedicines from the cultivation to the harvesting of the plants and the whole production cycle," Dr. Hülsermann explained.

Currently, the company has plantations in Europe, South Africa, and the United States, where plants are grown under controlled conditions that follow Good Agricultural Practice guidelines. To ensure maximum potency, Schwabe monitors the levels of plants' key active constituents throughout the growing season in order to harvest at the ideal time.

"High-quality raw plant materials are mandatory for the production of our unique phytomedicines," the website states. "Apart from the quality aspect, this also helps to avoid over-exploitation of wild populations of these medicinal plants and contributes to the conservation of biodiversity."

Schwabe's environmental stewardship is a value that remains an integral component of the company's operations. "As a company with a strong tradition and dedication to research, cultivation, and sustaining … nature's valuable resources, we are still following our founding father's philosophy," said Dr. Hülsermann. "So the sustainability of plants and their growing and harvesting are of utmost importance for us and our current and future business."

While the sustainable production of ingredients is key to securing future supplies, ensuring that affordable products reach as many consumers as possible is equally as important.

"An objective we all need to focus on within the herb and dietary supplement industry is to keep these products affordable and available wherever people are looking for them," said Devereux of Schwabe North America. "Our strategy is developing to serve not just the 300 million people in America, but worldwide, so we are learning every day more about consumer wants and needs in countries all over the world and how to create affordable solutions that support those wants and needs."

Dirk Reischig, PhD, Schwabe's chairman and CEO, explained how the company's founding values will continue to sustain the 147-year-old company.[3] "We believe that innovative phytomedicines will become increasingly important over the next few decades," he stated. "In the future, phytomedicines will help people, worldwide, to lead a sustainable, productive, and healthy life."

For a company that started with one man committed to harnessing and verifying the healing power of plants for consumer use, Schwabe's motto is particularly appropriate: "From Nature. For Health." HG

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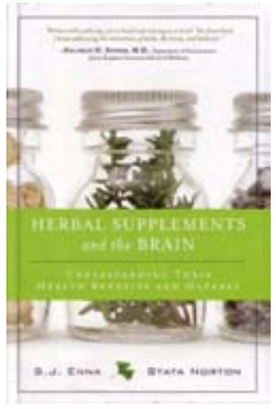
Schwabe quality assurance.
Photo ©2013 Schwabe

Herbal Supplements and the Brain: Understanding Their Health Benefits and Hazards by S.J. Enna and Stata Norton. Upper Saddle River, NJ: FT Press; 2012. Hardcover, 272 pages. ISBN: 978-0132824972. $34.99.

Herbal Supplements and the Brain is a rather unique book. While the subject matter is common to readers of *HerbalGram*, the fact that it's written by two leading mainstream pharmacologists is, I believe, a first. S.J. Enna, PhD, is a particularly well-known neuropharmacologist who has been the editor of several pharmacology journals and is a past president of the American Society for Pharmacology and Experimental Therapeutics. the late Stata Norton, PhD, was a professor emeritus in the University of Kansas Medical Center's Department of Pharmacology, Toxicology, and Therapeutics. As a pharmacologist myself, I was looking forward to the pharmacological perspective on these herbs.



The authors begin by reviewing the history of plants used as medicine, offering critiques along the way. Some inconsistencies nagged me from early on. In the history section, the authors claim that few botanical medicines were used by early humans for purposes similar to modern-day uses. Yet on the next page they acknowledge that a 30,000-year-old Neanderthal grave in Iraq revealed a medicine bag with flowers from six plants that are all used today for purposes that would have been very relevant to the cave man. They additionally assert that, in many cases, the active constituents of the plants are unknown, and that this makes it impossible to determine their effects in humans. This was a disappointing beginning and gave me the feeling that this viewpoint might carry on throughout the book. In a section on Hippocrates, there was discussion of how his humoral theory of disease held back the progress of medicine for hundreds of years. There was no mention of his statement that we should "let food be thy medicine and medicine be thy food." There was also no mention of his famous contributions on the ethics of medicine including the physician's oath "to abstain from doing harm."

Chapter 3 is about "thinking like a pharmacologist." While I have used this phrase myself, I must say that it felt uncomfortable to see the hubris present, and to read some of the tenants that I no longer hold to be "self-evident." In reference to modern drug development and regulation, for example, the authors state that "… it is not necessary for consumers to be concerned about the safety and effectiveness of prescription or over-the-counter medications." Wow... I'm not sure I ever believed that. I certainly don't believe it now, after 15 years of experience reviewing the safety and efficacy of prescription drugs. While there is much reductionist thinking in this chapter, there is useful information about how to approach the study of identifying useful chemicals in a plant. A particularly useful strategy that persists throughout the book is the importance of determining whether bioactive molecules in a plant actually are absorbed into the body after oral administration. This simple exercise often can eliminate many of the potential candidates for active constituents of a plant that were identified previously by *in vitro* test results. The authors go on to say that one must demonstrate the presence of the molecule in the brain as well. This seems a bit of a stretch since this is not required of synthetic compounds. The authors appear to suggest that a good scientist should deny evidence (*e.g.*, for sedation by a plant) that (1) has been used for this purpose for hundreds of years, and (2) that shows sedative effects in animals, unless and until we have positively identified a single component that reaches the brain in sufficient quantities and binds to a known brain receptor that could account for the pharmacologic property.

The next chapter drives this point home by discussing the brain as a "target" for medication. In covering the topic of neurotransmission, they suggest that a psychoactive drug must be shown to produce a measurable effect on a neurotransmitter receptor. My concern with this strategy is that it will produce only more drugs like the ones we already have. In a discussion of clinical trials, the authors propose that the crossover study is clearly the best design. In actuality, this is not the case, because crossover designs suffer from carryover effects and other problems of interpretation that limit their usefulness. Drs. Enna and Norton fail to mention the importance of an active control comparison in drug studies. If there is only placebo and test drug, the results cannot be interpreted unless there is a significant difference between the two groups. If neither treatment works, it is just as likely that the study design was poor as it is that the drug actually didn't work. A positive control that works and a negative control that doesn't (placebo) suggests you have a good study design that is capable of measuring the endpoint of interest. This is especially true for drugs that work on the central nervous system, where placebo rates as high as 50 percent are not uncommon.

Subsequent chapters deal with selected herbal medicines by reviewing their history, known chemistry, pharmacodynamics (drug action), and pharmacokinetics (drug absorption, distribution, metabolism, etc.). The chapters include the herbs *Ginkgo biloba* (Ginkgoaceae), St. John's wort (*Hypericum perforatum*, Hypericaceae), valerian (*Valeriana officinalis*, Valerianaceae), lemon balm (*Melissa officinalis*, Lamiaceae), kava (*Piper methysticum*, Piperaceae), lavender (*Lavandula angustifolia*, Lamiaceae), kudzu (*Pueraria montana*, Fabaceae), daffodil (*Narcissus pseudonarcissus*, Amaryllidaceae), passion flower (*Passiflora incarnata*, Passifloraceae), and tea (*Camellia sinensis*, Theaceae), as well as selected caffeinated beverages. I found the coverage of these to be very uneven. This was especially the case for phytomedicines that are the subject of thousands of publications such as ginkgo and St. John's wort. The vast literature was not evenly reviewed, and there were many missing references (that is, relevant statements were made without literature citations). Entire areas of relevant research and well-known research papers were unmentioned for these two herbs. While this is not surprising for authors who are not deeply experienced in this subject area, it was still disappointing as conclusions were being drawn without a basis in the available literature. On the other hand, the chapters dealing with lesser-researched plants (for which available literature could much more easily be grasped as a whole) seemed more comprehensive and thus more useful.

The title suggests that the purpose of the book is to understand the health benefits and hazards of plants acting on the central nervous system. I don't know of any book that has been able to accomplish this. It's a very tall order. For this purpose, there are other references that better review the literature, especially for ginkgo and St. John's wort. I do think the book has a niche, however. Readers with an advanced degree in the life sciences will be much happier with this book and will be able to relate to it. In my opinion, the pharmacologic detail will be out of reach for most laypeople and consumers.

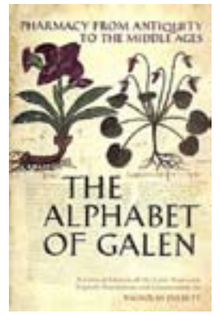
Those looking for a general reference guide or introduction to herbs will want to look elsewhere. And the sometimes condescending language that has found its way onto most pages may put off serious students of natural medicine. I absolutely agree that one must seek truth (if such a thing really exists in medicine) in an unbiased manner. But the scientist must realize that just because one explores truth on the molecular level, it does not mean that one is inherently free of bias, or that another's truth on a different level of organization is somehow less useful. Learning what questions to ask and in what order to ask them is a useful skill and can be practiced while reading this book. But again, it leads to a pre-specified end, *i.e.*, a single compound binding to a known receptor.

Mechanism of action is a highly interesting and useful tool. But I think we can expect that the pharmacologic effects (and mechanisms of action) of dietary supplements are going to be much more subtle than the ever more potent and selective world of synthetic pharmaceutics. If we are patient and keep an open mind, exploring these fascinating natural compounds will surely lead us to undreamed of systems, substrates, homeostatic processes, and epigenetic effects. The latter may begin to tell us what the things we eat are doing to us or for us.

—Jerry Cott, PhD
Pharmacologist, toxicologist
Silver Spring, MD

The Alphabet of Galen: Pharmacy from Antiquity to the Middle Ages – A Critical Edition of the Latin Text with English Translation and Commentary by Nicholas Everett. Toronto, Canada: University of Toronto Press; 2012. Softcover, 445 pages. ISBN: 978-0802098126. $95.00.

Galen (129–post 215 CE), also referred to as Galen of Pergamon (a Greek city-state in what is modern-day western Turkey), was a 2nd century naturalist philosopher and physician to the Roman emperors Marcus Aurelius and Commodus. Galen is credited with numerous writings as well as the development of alcohol (wine)-based botanical extracts (later known as "galenicals" in pharmacy), among many other accomplishments.



The *Alphabet of Galen*'s prologue claims to present "every medicine derived from minerals, as well as aromatics, and from every species of plants" — in all, some 220 plants, 61 minerals, and 19 animal drug products. This treatise is one of the more important pharmaceutical texts from the early Middle Ages, with surviving manuscripts from the 7th through 11th centuries. This important work has been little known until Nicholas Everett's thorough, competent study and English translation. The earliest manuscript, Everett finds, is probably from the region of Ravenna, Italy. Manuscript copies vary considerably, but the critical text is thorough and skillfully presented.

First, even though the treatise was published in the Kühn edition of "complete works" by Galen (20 volumes in 22 parts; Leipzig, Germany, 1821-1833), the text is not by Galen. The sources that the unknown author employed are as mysterious as the author's obscurity. Harnessing linguistics and the best tools available to modern scholars, Everett postulates that the author was learned in Greek as well as Latin and utilized sources that are now lost. The unknown author employed neither the Greek nor Latin works of the 1st century CE Greek physician and herbalist Dioscorides (an unexpected observation by Everett), nor closely followed any surviving classical texts. Everett also postulates (persuasively to this reviewer) that similarities to Dioscorides, Galen, and the Roman naturalist Pliny the Elder (23–79 CE) drew upon texts that probably included Sextius Niger's lost work on pharmacy, which Dioscorides and Pliny used as well. Thus, this popular work in Late Antiquity and the early Latin Middle Ages preserves plant and drug lore from "the ancient and most popular authorities," to quote from the epilogue (which itself may have been added to the text).

Most of the chapters' formats on plants have the following: (1) a brief description, origin, or location (with India

mentioned most frequently for more exotic plants); (2) a simple statement for most of the plants' general "properties" or virtues (such as "sharp, heating, and loosening properties" for cardamom [*Elettaria cardamomum*, Zingiberaceae]); and (3) uses and other applications primarily for medical afflictions. The author avoided (but not completely) what we would call superstition or magic, even more so than rational classical authorities such as Dioscorides and Galen. To us, verdigris (a green pigment) might or might not be good as an eye-salve, but it is bizarre when "some" mix it with an infant boy's urine, according to the text. Similarly, donkey dung mixed with vinegar "relives toothaches." These examples withstanding, the *Alphabet of Galen* is notable in the absence of what appears to us as truly irrational uses.

The book's alphabetical order served ease of use. Everett provides an excellent analysis of pharmacy in what he describes as "self-medicating in late Antiquity" and an implicit theory for associating properties with specific medicinal actions. For example, opium (derived from *Papaver somniferum*, Papaveraceae) has a "cooling" property that "alleviates earaches, reduces all types of fatigue in the body, and *for this same reason* it also induces sleep" (italics supplied). Similarly, licorice (*Glycyrrhiza glabra*, Fabaceae) has "moistening properties…therefore quenches thirst, and relieves pain in the kidneys and bladder." The connection between properties and specific medicinal applications is inconsistent, thus, for example, a cooling action rarely points to a specific medicinal affliction. Many plants have no properties specified.

The opium account delivers an objective, succinct description about harvesting, preparation, and adulteration, but omits the assertion by Dioscorides that "when too much of it is drunk, it plunges into a coma and it is deadly." "Uniquely," Everett finds, the *Alphabet of Galen* claims the best opium comes from Spain. Many therapeutic uses "hold up remarkably well against the finds of modern science," although some "seem to have no biological or physiological basis and remain puzzling," he writes. An example of what to us is rational, mastic gum (*Pistacia lentiscus*, Anacardiaceae), according to this book, "is styptic…It is good for those coughing up blood," whereas only recently have our laboratories proved it useful for peptic ulcer disease.

With an unknown author living in an unknown time and place and using many unknown sources, the *Alphabet of Galen* is an important, largely overlooked, and certainly unstudied treatise whose popularity mostly was confined to Late Antiquity and the early Latin Medieval West. Despite its title, it is not connected to Galen, which is a characteristic of the period's contrivance to lend authority to the composition. The original treatise was written in Latin, using "simple, technical language;" Everett's competent English translation achieves the same. The Latin and translation are on facing pages. Nicholas Everett's study is important for two primary reasons: to elucidate an important Western medical work on pharmacy, and — especially for *HerbalGram* readers — to establish a significant young scholar who can provide technical and linguistic skills to help us understand early herbal medicine.

—John M. Riddle, PhD
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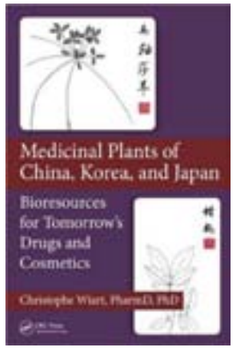
Available in the ABC Online Bookstore

Medicinal Plants of China, Korea, and Japan: Bioresources for Tomorrow's Drugs and Cosmetics by Christophe Wiart. Boca Raton, FL: CRC Press; 2012. Hardcover, 454 pages. ISBN: 978-1439899113. $149.95.

Medicinal Plants of China, Korea, and Japan is a compilation of botanical, chemical, and pharmacological information on roughly 200 selected plant species and is intended to be a reference for researchers who are looking for new leads from Chinese medicinal plants for pharmaceutical and cosmetic studies. Though Professor Stephen J. Hill, PhD, wrote in the preface that these plants "have been carefully selected for their novelty and pharmacological importance," no further explanation is provided in the text on why or how the plants were chosen for this work. Furthermore, the book contains no introduction, nor does it feature any concluding remarks.



The bulk of the book consists of nine chapters organized using the "Superorder" system proposed by the Angiosperm Phylogeny Group (APG) classification. They are Austrobaileyanae (ICBN family name: Austrobaileyaceae), Magnolianae (Magnoliaceae), Lilianae (Liliaceaea), Ranunculanae (Ranunculaceae), Rosanae (Rosaceae), Saxifraganae (Saxifragaceae), Santalanae (Santalaceae), Caryophyllanae (Caryophyllaceae), and Asteranae (Asteraceae). Under each Superorder are sections on selected orders and families. In each family section, brief morphological characteristics are given, followed by individual species.

The layout for each plant species is consistent, providing information on history (citation of the first botanical description of the plant), common names (mainly Malay, Chinese, Japanese, and/or Korean names), basionym (original Latin binomial), synonyms (Latin binomial), habitat in China and/or Southeast Asia, diagnosis (morphological descriptions of the plant species), medicinal uses and traditional and/or folkloric applications, pharmacology (brief description of selected *in vitro* and/or *in vivo* biological effects of the plant extract or its chemical constituents; in some cases, the structures of one or two major bioactive chemical constituents are provided); and finally, bioresources that includes promising bioactivity for further research. Major references are provided at the end of each chapter. The book concludes with five indices: common names, medicinal uses, natural products, pharmacological terms, and plants.

At first glance, I was attracted to this book's subtitle, *"Bioresources for Tomorrow's Drugs and Cosmetics*," because, as a researcher in the area of natural drug discovery, choosing which plants to study is critical to success. As the subtitle implies, the most interesting and useful information that a reader might look for is the pharmacological potential of each plant species. Indeed, the book's back cover asserts that "critical analyses of peer-reviewed articles provide the basis for Bioresource sections in each chapter wherein readers are advised, engaged, and guided toward exciting pharmaceutical and cosmetological research proposals." Unfortunately, the Bioresource section turns out to be one of the shortest sections in the text, containing only short phrases, such as "*In vitro* pharmacological study of alisol B monoacetate for its effect on cancer," or even as simple as "Antimalarial agent(s)." I find it disappointing that neither detailed explanations nor references are given to support these statements. In many cases, there are no clues at all to help a reader understand why a particular suggestion is made. For example, folicanthine from *Chimonanthus praecox* (Calycanthaceae) is proposed for study on Alzheimer's disease without any explanation. In another case, under the *Illigera appendiculata* (Hernandiaceae) entry, the author suggests "*In vitro* pharmacological study of actinodaphnine for its effect on acne," yet this compound never was mentioned as being present in this plant species.

The book seems to be full of confusing features. In numerous cases, partially highlighted chemical structures appear side-by-side with other structures bearing similar highlights. While the author never explains the meaning of these features, my suspicion is that he intended to illustrate the structural similarities between a plant constituent and a known active compound. For example, under the entry of *Illigera luzoniensis* (Hernandiacea), which contains actinodaphnine and *N*-methyl-actinodaphnine, the latter is recommendeded for *in vitro* study for its effect on alopecia, while the chemical structure of phenylephrine is given side-by-side. In my opinion, additional information and an expansion of the Bioresource section certainly would make the text more complete and useful. Moreover, it would be preferable if the author presented his views with sound scientific evidence.

On the back cover of the book, the author claims that "detailed photographs and hand-made botanical plates enable quick and reliable identification of each plant species." Unfortunately, no such plates can be found in the book. Each species is accompanied only by a hand-drawn line sketch of selected plant parts (not necessarily showing the medicinal part), from which minimal morphological information can be obtained for identification purposes.

Eight color pictures of plants appear in the middle of the book with no elucidation.

Overall, I am disappointed to find that the most important data I was looking for are missing from this book. If the author would consider a revision of this work, I suggest a substantial expansion of the Bioresource section by the inclusion of detailed explanations and literature citations.

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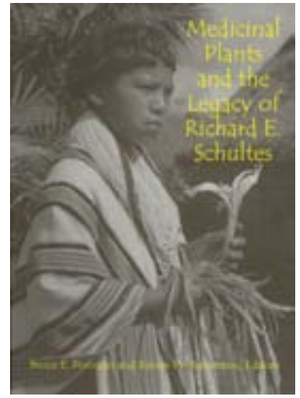

Available in the ABC Online Bookstore

Medicinal Plants and the Legacy of Richard E. Schultes edited by Bruce E. Ponman and Rainer W. Bussmann. St. Louis, MO: Missouri Botanical Garden; 2012. Softcover, 138 pages. ISBN: 978-0984841523. $24.95.

In the fall of 1977, as a new student at Harvard, I received some disturbing advice from a professor as I was attempting to select my PhD advisor. "Whatever you do, stay away from Richard Evan Schultes. He spent a decade alone in the Amazon, he is a dinosaur, and he is dangerous to otherwise good students."

Of course, the next morning I found myself in Professor Schultes' office at the Harvard Botanical Museum on Oxford Street. I found Dr. Schultes to be a highly cultured Boston Brahmin who was more proud of his graduation from Boston Latin School than any of his Harvard accolades. His knowledge of plants and botanical literature was encyclopedic, and he was deeply interested in the success of students. He certainly is one of the most extraordinary people that I have ever met in my entire life, and is universally considered to be the 20th-century pioneer of modern ethnobotany.

Although I cannot strictly claim the distinction of being a "Schultes student," having taken my PhD in evolutionary biology rather than ethnobotany, Professor Schultes

constantly encouraged me to pursue ethnobotanical studies in Polynesia during my other fieldwork there. Fortunately, I was accepted by his real students and regularly attended his seminars at the Botanical Museum. Dr. Schultes' students were an amazing lot, and nearly all of them went on to extraordinarily distinguished careers. The late Timothy Plowman, PhD, of Chicago's Field Museum and the late Calvin Sperling, PhD, of the US Department of Agriculture (USDA) were, in my opinion, two of the finest field botanists of the century.

Professor Schultes' surviving students have collaborated to produce a gem of a book, *Medicinal Plants and the Legacy of Richard E. Schultes*, which includes personal anecdotes, ethnobotanical research, and a great deal of biographical information. Reading this volume takes me back to my student days, when his graduate students — with me as a spare wheel — modestly divided up the entire planet into our own private research realms. On special occasions, Professor Schultes would show his 8 mm home movies of first contact with Amazonian tribes. Other days, we would discuss press reports of a real zombie walking into a hospital in Port-au-Prince, Haiti. Sometimes Albert Hofmann, PhD, inventor of LSD-25, would lecture us in organic chemistry. It was a heady experience. (For the record, Professor Schultes had no patience with fellow Harvard professor Timothy Leary, hippies, or recreational exploitation of indigenous psychoactive plants.)

The day that Professor Schultes discussed the molecular biology of the ayahuasca vine (*Banisteriopsis caapi*, Malpighiaceae) and chacruna (*Psychotria viridis*, Rubiaceae) in seminar was life-changing for me, and is the reason why I have devoted my career to the ethnobotanical search for new drugs. I realized that if indigenous people had discovered that level of sophisticated neurochemistry, somewhere a traditional healer just might hold the cure for cancer. Professor Schultes' deep respect for the dignity of indigenous peoples and his awe at their pharmacological achievements was inspiring.

Medicinal Plants and the Legacy of Richard E. Schultes is divided into 11 chapters. Michael Balick, PhD, begins with a deeply personal account of his introduction to Professor Schultes and documents the mentorship of the young Schultes as a student by Harvard Professor Oakes Ames. Rainer Bussmann, PhD — a co-editor of the book — documents the voluminous herbarium collections of Professor Schultes and his publication of 500 papers. My favorite part of his chapter is a photograph of the young Schultes in Oaxaca in 1938. Looking at the photographs, one can see how the dashing, brilliant, and compassionate young Schultes became a model for Hollywood characters ranging from Sean Connery's *Medicine Man* to Harrison Ford's portrayal of Indiana Jones.

An extremely tight chapter on Chácabo ethnobotany in Bolivia follows, written by Dr. Bussmann and Narel Zambrana. Distinguished ethnobotanist Robert Bye, PhD, ensues with an excellent analysis of Dr. Schultes' contributions to ethnotaxonomy, including an examination of his undergraduate work on the sacred plants of Mexico. Rodrigo Cámara-Leret, Zambrana, and Manuel Macía, PhD, continue with an excellent chapter on ethnobotanical techniques for the study of palms. Prospective students of ethnobotany would be well-advised to read this chapter carefully, including the appendices, as they prepare for their own field studies. Andrés Gerique contributed a chapter on the ethnobotany of the Ecuadorian Andes with fascinating analyses of plant use by the indigenous Shuar, the Saraguros, and the Mestizos, which reveals significant insights into land use and land tenure by different cultures.

Steven King, PhD, part of a company that recently scaled the Mount Everest of ethnobotany — successfully navigating a new botanical drug through the USDA (*i.e.*, the antidiarrheal drug crofelemer derived from the latex of the South American sangre de drago tree [*Croton lechleri*, Euphorbiaceae]) — devotes his chapter to how Professor Schultes inspired the creation of a major conservation effort, The Healing Forest Conservancy, and pioneered the concepts of benefits-sharing with indigenous people, long before the Convention on Biodiversity had been conceived.

Neil Schultes, PhD, Professor Schultes' son, shares some personal experiences about what it was like to grow up in the shadow of his famous father and to pursue a distinguished career in plant biology himself. He now perpetuates the pioneering Schultes spirit in his careful analysis of photosynthesis at the Connecticut Agricultural Experiment Station.

Distinguished plant explorer and expert in Asian ethnobotany, Doel Soejarto, PhD, reflects on the legacy of Richard Evan Schultes, sharing a marvelous photograph of himself and Professor Schultes in the Amazon in 1963. Dr. Soejarto, last year's recipient of the American Botanical Council's Norman R. Farnsworth Excellence in Botanical Research Award, humbly links his own remarkable achievements in exploring for new medicines from plants in Southeast Asia — including his discovery of the anti-HIV drug Calanolide A — to lessons he learned from Professor Schultes.

The penultimate chapter by Robert Voeks, PhD, Leaa Short, and Aline Gregorio evaluates the legacy of the journal *Economic Botany,* which was championed by Professor Schultes since its inception in 1947, illustrating how it has become increasingly internationalized and rigorous through the years.

The volume concludes with a magnificent chapter by James L. Zarucchi, PhD, of the Missouri Botanical Garden, which is replete with remarkable color photographs of Professor Schultes in Columbia. Deeply moving to me is his photograph of Professor Schultes and Arthur Sledge in England, at the grave of the 19th century Amazonian ethnobotanical explorer Richard Spruce.

Every student of ethnobotany, every firm that compounds plant medicines, and, indeed, every field biologist, should have a copy of *Medicinal Plants and the Legacy of Richard E. Schultes.* I pinch myself that I was so lucky to have had him as one of my mentors. By adding to this compilation the masterful biography of Dr. Schultes by Wade Davis, PhD, *One River* (Touchstone, 1996), any of Dr. Balick's books on ethnobotany or palm systematics, and perhaps

one of the popular books by Mark Plotkin, PhD, you will be able to come very close to the wonderful experience I had as a student with Professor Schultes.

— Paul Alan Cox, PhD
Institute for Ethnomedicine
Jackson Hole, WY

Palau Primary Health Care Manual: Health Care in Palau - Combining Conventional Treatments and Traditional Uses of Plants for Health and Healing by Stephen M. Dahmer, Michael J. Balick, Ann Hillman Kitalong, *et al*. Charleston, SC: CreateSpace Independent Publishing Platform; 2012. Softcover, 220 pages. ISBN: 978-1477446355. $40.95.

This book is the second healthcare manual produced by a multidisciplinary team of traditional healers, Western-trained healthcare workers, medical doctors, botanists, ethnobotanists, and local people — all engaged in the integration of conventional and traditional treatments and medicinal plants in Palau, Micronesia. The first volume, *Pohnpei Primary Health Care Manual*, was a groundbreaking book developed by some of the same visionary authors of this volume. This work and its predecessor are products of the New York Botanical Garden's Biodiversity and Human Health in Micronesia Program.

This Palau-focused volume is another gem of a book. It is so refreshing to read this book and to know that it is being distributed to communities as a tool to provide careful, respectful, and practical guidance on the application of some of the best therapeutic approaches to cross-cultural health and healing. I consider this book and approach to be the next step in the evolution of applied botany, ethnomedicine, ethnobotany, healthcare, and conservation. The Republic of Palau is the westernmost archipelago of the Caroline Islands in Micronesia, which are north of Irian Jaya and east of the Philippines in the geographic region of Oceania.

The people and institutions that created this book are a model for the future of integrated public health in biodiversity-rich nations. There are 18 authors and 36 local experts cited in the front of the volume — at least 54 people who collaborated to produce this publication. The institutional sponsorship includes the New York Botanical Garden, the Ministry of Health of the Republic of Palau, the Continuum Center for Health and Healing service of Beth Israel Medical Center in New York City, and the Belau National Museum in Palau.

As the back cover of *Palau Primary Health Care Manual* states so elegantly, "The Republic of Palau in the Caroline Islands has a traditional medical system developed over many generations. The *Palau Primary Health Care Manual* compiles traditional ethnomedical information about plants and presents it within the context of Western medicine." The book covers common health conditions, including some of specific interest to Palauan peoples, and provides information on approximately 80 plant species. According to the back cover, the healthcare manual "is intended as an educational manual for Palau and the Pacific region, an area where traditional medicine and some of the plants used in its practice, are endangered resources."

The book is divided into 12 chapters that describe various health conditions and combine current Western medical knowledge with traditional Palauan botanical treatments; pharmacological efficacy and toxicity of each species also are included if such data exists in the literature.

The specific chapters focus on the following: preventive medicine in Palau (which is quite profound and well-articulated); chronic diseases (such as heart disease, cancer, and diabetes); bites and stings; gastrointestinal disorders; skin disorders; cuts, wounds and broken bones; stress; pain; women's health; men's health; colds and flu; and finally, ear, nose, and throat issues. Each chapter contains multiple color photographs of the plants described, including, in most cases, details of the flower, fruit, root, or plant part that is used in ethnomedicine. Information on a particular plant used in traditional medicine typically includes local and scientific names, a description of the plant, habitat ranges of the plant, traditional use, and pharmacological properties and toxicology.

A list of voucher specimens linked to the plants also is provided. I was especially impressed by the 21-page bibliography, which will be useful to any specialist interested in following up on any of the information presented.

Overall, this is an excellent book that hopefully will inspire other local and international research consortiums to produce similar volumes. There has been a great deal of focus and concern in many sectors about the inappropriate use of traditional medical knowledge in the past decade. This publication represents the opposite: a highly integrated applied focus on enhancing and managing health of communities utilizing the best of all medical traditions and knowledge. I would love to see ethnobotanists, traditional healers, medical doctors, nurses, public health workers, community health specialists, graduate students, government agencies, and international funding agencies focus on the production of manuals like this to assist countries and communities in both the conservation and utilization of their biocultural diversity and management of community health. It is then that people working in the abovementioned disciplines and organizations will want to own this book. This volume could be employed to stimulate discussion among communities and governments in other geographic regions of the world about what sort of manual would be most effective for that culture and region.

—Steven R. King, PhD
Sr. Vice President, Sustainable Harvesting and Ethnobotanical Research
Napo Pharmaceuticals, Inc.

Timothy J. Motley 1965–2013

Timothy Motley, PhD, described by his friends, colleagues, and family as a gifted and well-loved tropical botanist and explorer, passed away on March 28, 2013, at the age of 47. Motley was the J. Robert Stiffler Distinguished Professor of Plant Science at Old Dominion University (ODU) in Norfolk, Virginia, where he taught a popular ethnobotany course, along with four other plant science courses, in the same department as his wife, Tatyana Lobova, PhD. Dr. Motley also served as the director of science at the Norfolk Botanical Garden (NBG).

"Tim was not only a gifted scientist, field botanist, and collaborator, but also a friend who loved life, work, his family, and plants," wrote Edward J. Kennelly, PhD — a collaborator of Dr. Motley's and a professor at Lehman College, City University of New York — in an email to colleagues shortly after Dr. Motley's passing. "In our fieldwork that took us from nearby Pound Ridge, New York to collect black cohosh [*Actaea racemosa*, Ranunculaceae], to remote areas of Yunnan, China (to collect anything), I grew to know Tim better, and I valued greatly our time together, both for the science and camaraderie."

In 2006, Drs. Motley and Kennelly received a grant from the National Institutes of Health's National Center for Complementary and Alternative Medicine to study black cohosh and its related species. The same year, Dr. Motley joined ODU's Department of Biological Sciences and became the director of science at NBG.

Aside from being a professor and research scientist, Dr. Motley had a passion for the flora of the Pacific islands and regularly traveled to remote regions of the world to study plants. His research took him to exotic locales including the Kingdom of Tonga, Tahiti, New Caledonia, Pohnpei, Rapa Iti, Fiji, Papua New Guinea, Mauritius, and the Galápagos archipelago, among many others. His love of botanical exploration began while he was still in school.

"Tim got interested in botany and especially ethnobotany when he was an undergrad at Eastern Illinois University. … Later, at the University of Hawaii, he was working on [his] PhD with Dr. Gerald Carr and he fell in love with the Pacific island flora," noted his wife, Tatyana, in an email (April 16, 2013). "His advisors played a very important role in defining his botanical interests and shaping his research, and he was very grateful how generous they were with sharing time and knowledge."

Dr. Motley met Tatyana while they were working at the New York Botanical Garden (NYBG). From 1998 until 2006, Dr. Motley held various positions at NYBG, including assistant curator, acting department chair, and associate curator of The Lewis B. and Dorothy Cullman Program for Molecular Systematics Studies — a research body that focuses on "addressing questions of plant classification, historical biogeography, plant-animal interactions, and character evolution."[1]

"I started working [at NYBG] as a postdoc but [didn't] meet Tim for six months or so because he spent a lot of time in the field," said Tatyana. "Later it turned out that we were living in the same apartment building near the Garden. He was an amazing person — very kind, generous, funny, and very honest and reliable."

Scott Mori, PhD, the Nathaniel Lord Britton Curator of Botany at NYBG, first met Dr. Motley in 1996 and became friends with him and Tatyana. "I was impressed with the breadth of Tim's interest. He was not only a … botanist but also a plant systematist who specialized in Rubiaceae. He used both morphological and molecular data to study the phylogeny of this family [and] was a botanical explorer [who] headed the American side of a collaborative project with China," said Dr. Mori (email, April 9, 2013).

During his time at ODU, Dr. Motley became known for his course on ethnobotany and for his contagious passion for botany.

"Tim's ethnobotany course always filled as soon as registration opened," said Dr. Lytton John Musselman, the Mary Payne Hogan Professor of Botany at ODU, and a colleague of Dr. Motley's (email, April 9, 2013). "He had a gift for linking the use of a plant with its biology and did it in a clear, effective and challenging manner. … A clear reflection of this botanical magnetism was the establishment of a botany club on our campus. Few campuses have this claim."

Whether Dr. Motley was studying plants of remote Pacific islands, teaching students at ODU, or conducting research with colleagues, Dr. Motley's colleagues said that he will be remembered as a loving husband, father, and an accomplished scientist and mentor.

"He said many times that his professors were very good to him and he wanted to help [his students] as much as he could," said Tatyana. "All of Tim's former students are also his good friends. I think that friendship was very important to him. I think he was exactly the same in any setting — just himself — kind, easy going, and funny."

In addition to his wife, Dr. Motley is survived by his two-year-old son, Anton. A memorial service for Dr. Motley was held at the Norfolk Botanical Gardens on May 17, 2013. HG

—Tyler Smith

Reference

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Billy Joe Tatum
1932–2012


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Wild foods expert, international epicurean gourmand, herbalist, and author, Billy Joe Tatum of Melbourne, Arkansas, passed away on March 26, 2012, at the age of 80. She was born February 15, 1932. Billy Joe won a reputation as the successor to Euell Gibbons (1911-1975), who generated interest in wild foods with popular books such as *Stalking the Wild Asparagus* (Alan C. Hood & Co., Inc., 1962).

Billy Joe's 1976 bestseller, *Billy Joe Tatum's Wild Foods Cookbook & Field Guide* (Workman Publishing Co., Inc.), elevated Gibbons' wild food foray from the campfire to the gourmet kitchen, raising the perception of wild edibles from simple survival food to epicurean art. She hosted numerous gourmet wild food dinners. For example, the late Winthrop P. Rockefeller, Jr., won the winning bid on a Billy Joe Tatum wild foods feast at a 1979 arts fundraising auction. Guests included Arkansas notables such as Bill and Hillary Clinton — Arkansas governor and first lady, at that time — who were treated to elderberry and blackberry aperitifs followed by watercress soup, apple-spearmint salad, pheasant liver paté, elderberry capers, hickory-nut-stuffed eggs, and venison Wellington.

Soon after publication of her first book, Billy Joe and her physician husband, Harold "Hally" Tatum, MD, were featured in the first chapter of the 1977 National Geographic classic *Nature's Healing Arts*.[1] An inexhaustible bouquet of energy and ideas, Billy Joe's vivacious writing was inspired by her philosophy that "the only way to make life fun is to make it a game. I found excitement in the endless possibilities of wild foods."[2]

Her fame grew with several appearances on "The Johnny Carson Show" and with TV host Dinah Shore. Personality profiles featuring Tatum appeared in numerous magazines including *People*, *National Geographic,* and *Gourmet.* She took on the persona of an Ozark granny-herbalist (though just in her 40s), with a gray-flecked, waste-length braid decorated with an ever-present buzzard feather, while sporting a corncob pipe.

Billy Joe graduated from Ouachita Baptist University in Arkadelphia, Arkansas, with a degree in music. She eschewed a Julliard scholarship and career track toward the Metropolitan Opera to marry in 1951. In 1958, after several years in Detroit, the couple decided to return to their native Arkansas. They took out a map, closed their eyes and randomly pointed a finger toward the Ozarks. The finger landed on the map near Melbourne, in Izard County, Arkansas, an Ozark hamlet in need of a physician. In 1958, Dr. Tatum opened a rural practice there. At their famed Ozark mountaintop home, "Wildflower," they raised five children.

Dr. Tatum noted home remedies on his patients' charts, and eventually he and Billy Joe collected over 2,500 of these from community members. Until the mid-1970s, even state highways in this remote Ozark location were gravel roads. Home remedies were normal medical practice.

"One of my first remembrances of learning remedies from a patient is the day I trekked into Harold's office with all four kids in tow," Billy Joe once shared. "I was just absolutely worn to a frazzle by having a houseful of kids with colds and runny noses."

Her husband was so tired each day after practicing medicine that she didn't want to bother him with their own children's runny noses.

"But that day, feeling so frazzled, I decided I would try a trick of the doctor's wifery; I would just go and sit in the front of the office and wait for an appointment. And that was the day I happened to meet up with Aunt Tenny. This little old lady started talking to me and invited me to her house and made me a wonderful cup of soothing tea. Before long, she had convinced me that I should drink calming teas, give the children catnip [*Nepeta cataria*, Lamiaceae] for sleeplessness and dittany [tea; *Cunila origanoides*, Lamiaceae] to lower temperature..., but Aunt Tenny made me realize that it was very important to put children's tea in a beautiful, little china cup with a pretty picture on it. She knew all the secrets."[3]

Billy Joe became the acknowledged expert on Ozark folk medicines in addition to being an internationally recognized specialist in wild foods. She is survived by her husband, her five children, nine grandchildren, five great grandchildren, three siblings, and two generations of artists, dancers, musicians, writers, photographers — the famous and the obscure — whom she generously entertained and often housed at the Tatums' Ozark home. This writer is among those who experienced that expansive generous spirit. HG

—Steven Foster

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Paederia foetida (Rubiaceae)

This climbing liana grows as a weed on several Indian Ocean islands, including Comoros, Madagascar, and the Mascarenes. Despite *P. foetida*'s sulphur-fecal-like odor, similar to that of other species in its genus, it is commonly ingested and applied to the body for its anti-inflammatory properties. In the traditional medicine systems of these islands, leaf preparations are rubbed on wounds to stop bleeding as well as ingested to treat eczema and to prevent indigestion and upper abdominal pain. The whole plant is consumed for gastric pain and bladder and digestive complaints in addition to being administered as a bath to heal skin irritations and venereal diseases.

Adapted from *Medicinal and Aromatic Plants of Indian Ocean Islands* by Ameenah Gurib-Fakim and Thomas Brendler (MedPharm, 2004). Photo ©2013 Gurib-Fakim.

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