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SPECIAL ISSUE

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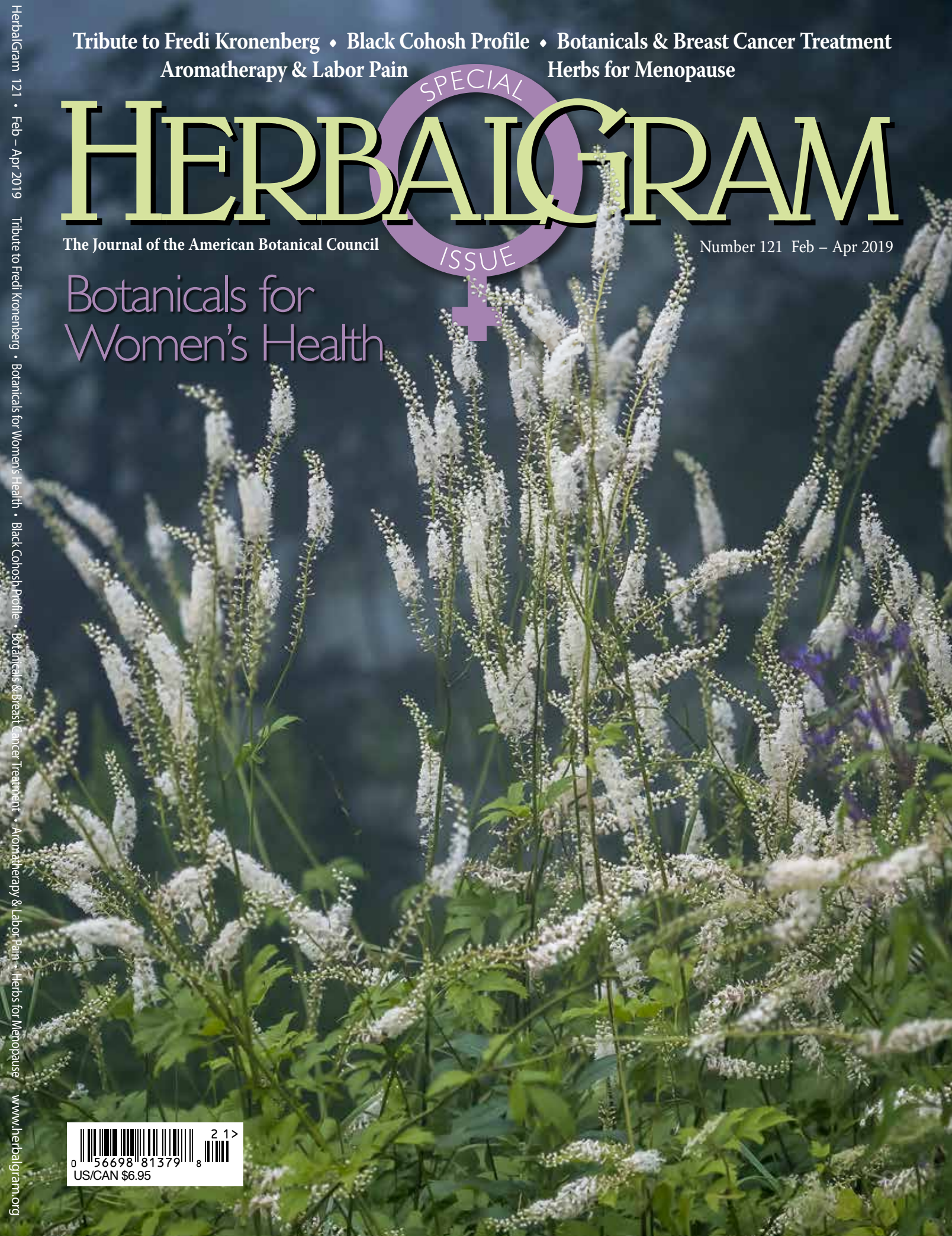
Botanicals for Women's Health



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dear *reader*

This themed issue of *HerbalGram* explores "Botanicals in Women's Health" and is dedicated to the memory of Fredi Kronenberg, PhD. Fredi was a passionate researcher and advocate of botanical medicines and their applications in women's health. She co-founded the Richard and Hinda Rosenthal Center for Complementary & Alternative Medicine at Columbia University, the first center for research and education in complementary and alternative medicine funded by the National Center for Complementary and Integrative Health. Among her numerous positions and affiliations, Fredi served on the Board of Trustees of the American Botanical Council for 18 years.

We are deeply grateful to our good friends, colleagues, and longtime ABC Advisory Board members Aviva Romm, MD, and Tieraona Low Dog, MD, who have volunteered their time as guest editors of this special issue. In addition to helping edit most of the articles in the issue, they have written a guest editorial in a question-and-answer format in which they discuss their perspectives on the use of botanical medicines in women's health and the overall state of herbs and phytomedicines in clinical medicine. Both Aviva and Tieraona have written highly respected books on the subject of herbs in women's health, and both have been chosen to receive ABC's newest award, the ABC Fredi Kronenberg Excellence in Research and Education in Botanicals for Women's Health Award.

We also include a personal tribute to Fredi from two of her closest friends and colleagues, Adriane Fugh-Berman, MD, and Christine Wade, MPH. They share some stories of their relationships with Fredi and some insights into the depth of Fredi's intellectual curiosity as a scientist and researcher.

We offer our deep gratitude to Lise Alschuler, ND, another valued member of the ABC Advisory Board, who has contributed an article on the role botanical medicines can play as adjunct therapies during and after breast cancer treatment. Lise is an expert on this subject; she has a clinical practice that specializes in natural treatments in oncology and is a breast cancer survivor herself.

In this issue, we present memorial tributes to numerous friends and colleagues who have contributed to the natural products community and industry in various significant ways: Barbara "BJ" Johnston, managing editor of *HerbalGram* for 17 years, from 1983 to 2000; Brian Keating, the brilliant herb and quality tea expert; herb and ginseng pioneer Gary Raskin, with whom I often worked when we both started our fledgling herb distributing businesses in the mid-1970s; Peter Semper, a visionary, dietary supplements industry pioneer, and public relations and political strategist; and Professor Rudolf Hänsel, a leader in German phytomedicinal education and author of several leading textbooks, some of which inspired countless scientists, including our own chief science officer, Stefan Gafner, PhD. Each year, it seems that more and more of the people we memorialize in these pages have made major contributions not only to the scientific research and education community, health professions, and herb industry in general, but also to ABC and *HerbalGram*. And, even though they have passed on, their contributions ensure that they remain important parts of our community and our individual lives.

And finally, in the errors and omissions department: In our last issue, we included an article on herb and other natural products companies that have become B Corporations, a certification that represents a company's dedication to the public good, commitment to sustainable practices, and much more. Although our article was intended to be comprehensive, but not necessarily exhaustive, we inadvertently overlooked Herbalist & Alchemist (H&A), an herbal tincture company founded by our good friend and longtime ABC Advisory Board member David Winston. H&A has been a B Corp since 2010. We genuinely lament the omission.

Mission: Provide education using science-based and traditional information to promote responsible use of herbal medicine—serving the public, researchers, educators, healthcare professionals, industry, and media.

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

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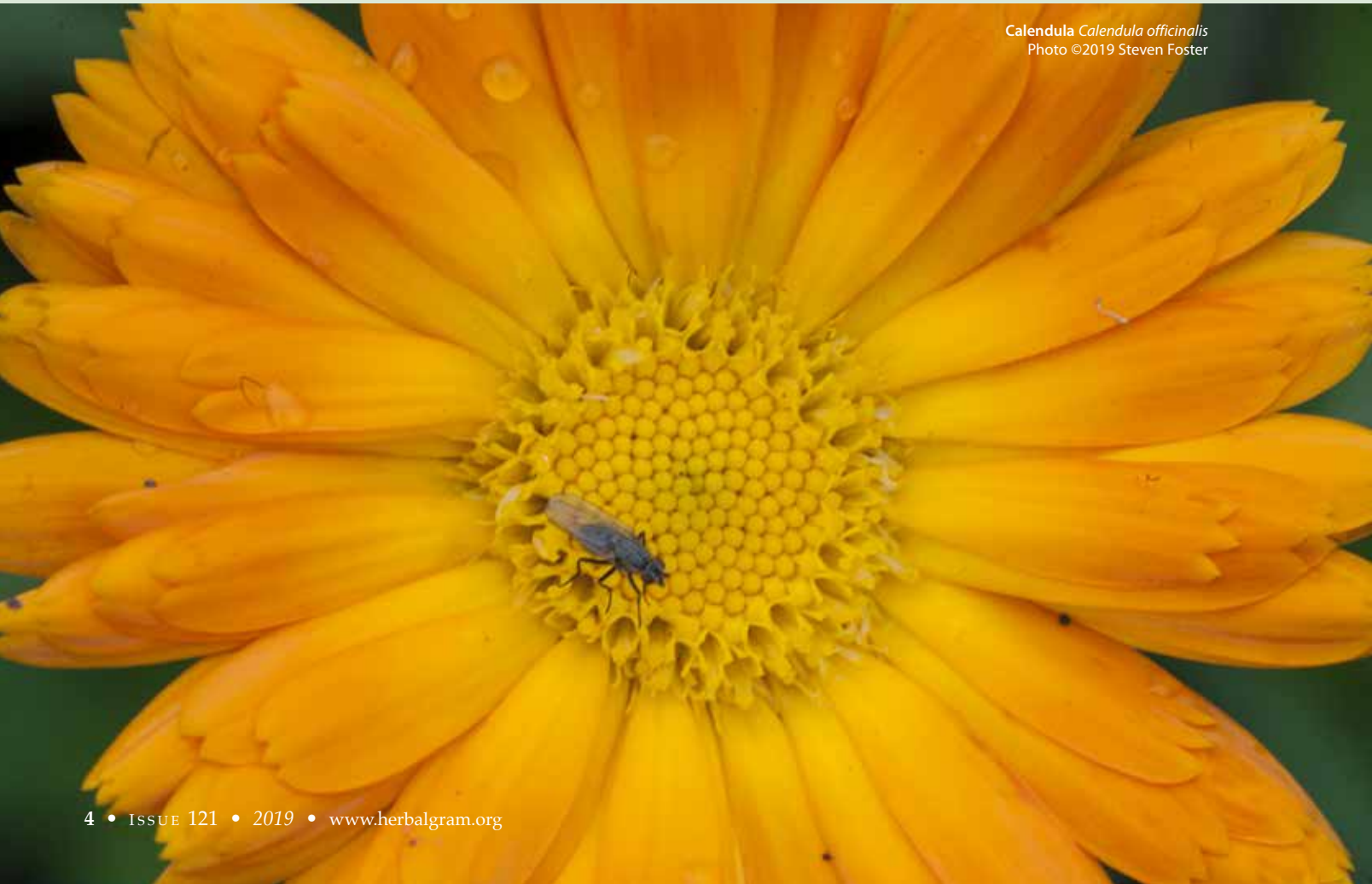

Calendula *Calendula officinalis*
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departments

On the Cover
Black cohosh *Actaea racemosa* at Avena Botanicals, Rockport, Maine.
Photo ©2019 Steven Foster

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Black Cohosh

***Actaea racemosa* (syn. *Cimicifuga racemosa*)**

Family: Ranunculaceae

INTRODUCTION

Native to eastern North America, black cohosh (*Actaea racemosa*) is an erect perennial in the buttercup (Ranunculaceae) family that reaches four to eight feet in height and has long, wand-like white flowers with numerous showy stamens.[1] It is found in rich soils on wooded hillsides of deciduous forests, particularly in Appalachia, and occurs in 25 US states and Ontario and Quebec, from Massachusetts and southern Ontario, to Illinois and Missouri, south to Arkansas and central Alabama, through Georgia and South Carolina.[2,3] Black cohosh, the article of commerce, is defined in the *United States Pharmacopeia* (USP) as the dried rhizome and roots of *A. racemosa*, containing not less than 0.4% of triterpene glycosides.[4]

Almost all of the commercial supply of black cohosh rhizome comes from wild collection. Based on 14 years of tonnage surveys carried out by the American Herbal Products Association, at least 3,830,117 lbs (dry weight basis) of black cohosh were harvested from 1997 through 2010, of which 72,751 lbs (1.9%) were produced through cultivation and 3,757,366 lbs (98.1%) were wild collected.[5,6] There is some commercial wild collection under US Department of Agriculture (USDA) organic certification regulations in Kentucky, North Carolina, and West Virginia, as well as cultivation in Maine, Missouri, New York, Oregon, and Virginia.[7]

This article concerns black cohosh only and does not refer to the other botanical species traded with the common name "cohosh," such as blue cohosh (*Caulophyllum thalictroides*, Berberidaceae), yellow cohosh (*A. podocarpa*),[8] red cohosh (*A. rubra*), or white cohosh (*A. pachypoda*).[9,10]

HISTORY AND CULTURAL SIGNIFICANCE

HerbalGram issue 45 (1999) includes a comprehensive review by Steven Foster that elaborates on the complicated etymology, taxonomy, ethnobotany, and botanical history of black cohosh,[1] which will not be repeated in this profile.

The genus name *Actaea* is derived from the Greek ακτέα, meaning "elder tree," because *Actaea* foliage was believed to resemble that of *Sambucus nigra* (Adoxaceae). The previously used genus name *Cimicifuga* is derived from the Latin *cimex*, meaning "bug," and *fuga*, meaning "flight," due to the observation that *Cimicifuga* species appear to repel bugs,[11] which also explains black cohosh's other common name, bugbane. The term "cohosh" is an indigenous term of uncertain meaning but was used for four different plants: the aforementioned black, blue, red, and white cohoshes.[12] Black cohosh is a traditional Native American medicine described and used by eastern North American tribes including the Cherokee, northeastern Algonquian, and Oklahoma Delaware.[1] According to Eclectic pharmacist John Uri Lloyd (1849-1936), indigenous applications that were introduced to early American medical practice included an aqueous decoction

preparation for "diseases of women, for debility, to promote perspiration, as a gargle for sore throat, and especially for rheumatism."[13]

New York colonial politician and natural scientist Cadwallader Colden (1688-1776) used the Latin name *Actaea racemis longissimis* and common name "black snakeroot" to refer to black cohosh in his 1742 work *Plantae Coldenhamiae*, which was later used by Swedish botanist Carl Linnaeus (1707-1778) in the 1749 edition of *Acta Societatis Regiae Scientiarum Upsaliensis* ("Proceedings of the Royal Society of Science at Uppsala").[14] Colden's monograph described therapeutic applications in the form of a cataplasm (poultice) for *tumores scirrhosos* (scirrhous tumors) and a tincture of the root for *languor, lassitudine spontanea* (lack of energy, weakness, spontaneous lassitude). Letters sent by Colden to English botanist Peter Collinson (1694-1768) in 1743, and to German botanist Johannes Fredericus Gronovius (1690-1762) in 1744,[15] took aim at what he believed were errors made in Linnaeus' 1737 work *Genera Plantarum* concerning characteristics of the genus *Actaea*.[16] Subsequently, the botanical name *Actaea racemis longissimis* with the pharmacopeial name "Actaea radix" appeared in Linnaeus' 1749 work *Materia Medica*, which listed Virginia as the source of the plant and ascribed sudorific (sweat-inducing) action and medical use for treatment of *asthenia virginica*,[17] a "disease formerly much noticed in Virginia."[18] The genus and species *Actaea racemosa* appeared four years later in Linnaeus' 1753 *Species Plantarum*, wherein he wrote that the species' habitat was Florida, Virginia, and Canada.[19]

German botanist Frederick Traugott Pursh (1774-1820) later renamed the plant *Cimicifuga serpentaria* with the common name "black snake-root" in his 1814 *Flora Americae Septentrionalis*, providing a brief description of its habitat: occurring in shady, stony woods from Canada to Florida.[20] Soon after, English botanist Thomas Nuttall (1786-1859) named it *Cimicifuga racemosa* in his 1818 work *The Genera of North American Plants*, in which he posed a question, as if he were doubting his own naming convention: "Does this exceptionable plant belong indeed to Cimicifuga?—A North American genus."[21] One hundred and eighty years later, in 1998, *C. racemosa* was reclassified as Linnaeus' original name, *Actaea racemosa* L., based on DNA analysis.[22]

Black cohosh *Actaea racemosa*
Photo ©2019 Steven Foster

In 1820, "Cimicifugae Radix" appeared on the secondary list of substances in the first publication of the USP, with Pursh's botanical name *Cimicifuga serpentaria* and the common name "black snake root."[23] The USP secondary list was like a pharmacopeial purgatory, providing a temporary place for "medicines little employed or of doubtful value" that could either be elevated to the primary list in the next revision of the pharmacopeia or degraded toward omission. Ten years later, in the first decennial revision (USP 1 1830), two Latin binomials were listed, the first with Linnaeus' genus (*Actaea*) misspelled as *Actea racemosa* followed by Pursh's *C. serpentaria* as a synonym. Its properties were listed as "odour unpleasant; taste bitter, nauseous," and its medical actions as "astringent, diuretic, sudorific, subtonic."[24] Cimicifugae Radix was elevated from the secondary list to the primary list in the second decennial revision (USP 2 1840), this time using Nuttall's botanical name *C. racemosa*, erroneously attributing the name to American botanists John Torrey (1796-1873) and Asa Gray (1810-1888).[25] *Cimicifuga* remained official up through the 10th decennial revision (USP 10 1920).[4]

In 1833, a monograph titled "Cimicifuga, U.S. Secondary, Black Snakeroot" was included in the first edition of the *Dispensatory of the United States of America* (USD 1 1833) with the botanical names *C. racemosa* and *C. serpentaria*.[26] The USD monograph described its medicinal actions and uses as:

> Cimicifuga unites, with a tonic power, the property of stimulating the secretions, particularly those of the skin, kidneys, and pulmonary mucous membrane. It is thought also by some to have a particular affinity for the uterus. Its common name was probably derived from its supposed power of curing the disease arising from the bite of the rattlesnake. It is employed chiefly in domestic practice as a remedy in rheumatism, dropsy, hysteria, and various affections of the lungs, particularly those resembling consumption. The form of decoction is usually preferred. An ounce of the bruised root may be boiled for a short time in a pint of water, and one or two fluidounces given for a dose several times a day.

In 1888, "Fluid Extract of Cimicifuga" was included as a component of an "unofficinal" preparation called *Syrupus Actæa Compositus ("Compound Syrup of Actaea, Compound Syrup of Cimicifuga (or Black Cohosh)"),* monographed in the first issue of the American Pharmaceutical Association's *National Formulary* (NF I).[27] Cimicifuga NF remained in the USD until the 25th edition, published in 1955.[28] In this edition, the USD appeared to dismiss black cohosh by paraphrasing a 1932 paper published in the *Journal of the American Pharmaceutical Association*, which had concluded "that there was no pharmacologic evidence of any therapeutic value of cimicifuga."[29] The USD monograph referred to the eighth edition of *The National Formulary* (NF VIII 1946) wherein Fluidextract of Cimicifuga and Tincture of Cimicifuga had been official preparations.[30]

In the early 19th century, case reports of successful use of black cohosh to treat chorea (an abnormal involuntary movement disorder) occasionally appeared in the medical literature. Seven case reports from the early 1830s were described in a paper by Dr. Thomas Story Kirkbride (1809-1883) of Philadelphia in *The American Journal of the Medical Sciences*.[31] Two case studies written by Dr. L.T. Wootten of Lunenburg, Virginia, describing successful treatment of chorea with preparations of powdered black cohosh mixed in syrup of molasses and tincture ("1 oz. of cohosh to 1 pint of good rye whiskey") were published by Dr. T.J. Garden in the *Southern Medical and Surgical Journal*.[32]

The longest marketed medicinal product containing black cohosh is "Lydia E. Pinkham's Vegetable Compound," which was brought to market in 1875 by Lydia Estes Pinkham (1819-1883), the founder of the Lydia E. Pinkham Medicine Company (Lynn, Massachusetts). A reformulated version of the product is still available today as an herbal dietary supplement (Lydia Pinkham® Herbal Compound) from Numark Laboratories (Edison, New Jersey). In 19th-century United States, when terms like "menstruation," "uterine inflammation," and "painful monthly periods" were rarely spoken out loud, these terms were used in the advertising of the product. The original formulation called for 8 oz aletris (*Aletris farinosa*, Nartheciaceae) root, then referred to as unicorn root, 6 oz life root (*Senecio aureus*, Asteraceae), 6 oz black cohosh, 6 oz pleurisy (*Asclepias tuberosa*, Apocynaceae) root, 12 oz fenugreek (*Trigonella foenum-graecum*, Fabaceae) seed, and enough alcohol (18% alcohol by volume [ABV]) for 100 pints. For 1,000 bottles of compound, 27 gallons of alcohol were used.[33]

After Pinkham died in 1883 at age 64, her husband, Isaac, and two of their children, Charles and Aroline, continued to run the business. At the time of Lydia's death, the company had annual sales of about $300,000. By 1925, the Pinkham Medicine Company had about 450 employees with annual sales of about $3.8 million. Lydia's great grandson Charles "Charlie" Pinkham was treasurer when the Pinkham family sold the company in 1968 for more than $1 million to Cooper Laboratories, Inc. of Connecticut, after which production was moved to Puerto Rico.[34] In 1987, Numark Laboratories, the current marketer, acquired a license to market the Lydia Pinkham formulations.[35] The Lydia Pinkham House in Lynn was added to the National Park Service's National Register of Historic Places in 2014.[36]

In 1982, the US Food and Drug Administration (FDA) considered inclusion of black cohosh as an active ingredient in its proposal to establish a monograph for over-the-counter (OTC) menstrual drug products. The FDA review panel evaluated one existing drug, the aforementioned Lydia E. Pinkham's Vegetable Compound, although the formula had changed since the 19th century. The FDA-evaluated formulation contained fluidextracts of black cohosh in combination with extracts of Jamaican dogwood (*Piscidia erythrina*, Fabaceae), pleurisy root, life root, dandelion (*Taraxacum officinale*, Asteraceae) root, gentian (*Gentiana lutea*, Gentianaceae) root, and licorice (*Glycyrrhiza glabra*, Fabaceae) root. While the agency acknowledged the 150-year history of apparently safe use of black cohosh fluidextract, the FDA stated that no human studies were available on its individual effectiveness in the treatment of primary dysmenorrhea, and therefore classified it in category II, meaning not Generally Recognized as Safe and Effective (GRASE) as an active ingredient of OTC menstrual drug products.[37] In 1988, in a subsequent "tentative final monograph" for OTC menstrual drug products, black cohosh remained listed in category II.[38] Four years later, the FDA proposed that black cohosh should be classified as not GRASE for use as an active ingredient of orally administered menstrual drug products,[39] and passed a final ruling to that effect in 1993.[40]

In 1989, the German Commission E authority published a positive monograph for black cohosh (*Cimicifugawurzelstock* – "Cimicifugae racemosae rhizoma"), prepared as an extract (at daily dosage corresponding to 40 mg of dried rhizome) for "premenstrual discomfort, dysmenorrhea or climacteric [menopausal] neurovegetative ailments."[41] After

a 70-year pause, in 2001, a proposal was made for black cohosh rhizome to reenter the USP along with additional new monographs for the fluidextract and dry extract forms.[42] Six years later, the new monographs became official in the second supplement to the 30th revision (USP 30 2007).[43] In 2002, a comprehensive monograph (quality and therapeutics) for "Rhizoma Cimicifugae Racemosae" entered volume two of the *WHO Monographs on Selected Medicinal Plants*.[44] In 2010, and in its 2018 update, the European Medicines Agency (EMA) published a labeling standards monograph for black cohosh that superseded the German Commission E monograph.[45]

CURRENT AUTHORIZED USES IN COSMETICS, FOODS, AND MEDICINES

In the United States, black cohosh may be used as a component of dietary supplement products, which require FDA notification within 30 days of marketing if a structure-function claim is made and product manufacturing that adheres to current Good Manufacturing Practices (cGMPs).[46]

In Canada, black cohosh is regulated as an active ingredient of licensed natural health products (NHPs), which require pre-marketing authorization from the Natural and Non-prescription Health Products Directorate (NNHPD). Labels of licensed NHPs prepared from USP-quality black cohosh may carry these claim statements: "Used in Herbal Medicine to help relieve muscle and joint pain associated with rheumatic conditions (such as rheumatoid arthritis, osteoarthritis, and/or fibrositis), and of pain associated with neuralgia (such as sciatica)"; "Used in Herbal Medicine to help relieve the pain associated with menstruation"; "Used in Herbal Medicine to help relieve premenstrual symptoms"; and "To help relieve symptoms associated with menopause." Regarding quality specifications, the NNHPD monograph states: "The medicinal ingredient may comply with the specifications outlined in the Black Cohosh, Black Cohosh Fluidextract, Powdered Black Cohosh, Powdered Black Cohosh Extract, or the Black Cohosh Tablets Monographs published in the US Pharmacopeia."[47]

In the European Union, black cohosh dry extract may be used as an active ingredient of licensed well-established use herbal medicinal products (WEU-HMPs) labeled with the therapeutic indication "for the relief of menopausal complaints such as hot flushes and profuse sweating."[45]

Black cohosh *Actaea racemosa*
Photo ©2019 Steven Foster

MODERN RESEARCH

Triterpene glycosides,[48] primarily actein and cimigenol-3-*O*-xyloside, are considered to be the primary and characteristic constituents of black cohosh rhizome. In addition, 27-deoxyacetylacteol and other aglycones have been detected. Cimigenol-3-*O*-arabinoside has been proposed as a species-specific marker.[49] Another important component class is the cinnamic acid esters, including fukinolic acid and the cimicifugic acids A, B, E, and F. Minor constituents include caffeic acid, ferulic acid, isoferulic acid, salicylic acid, tannins, resins, fatty acids, starch, and sugar.[50] The identity of the primary active ingredient(s) is a subject of contention in the literature and of ongoing investigations. The isoflavone formononetin,[51] a long-suspected active compound, could not be detected in black cohosh plants, the botanical drugs, or in extracts (isopropanolic/ethanolic aqueous or methanolic) when researchers analyzed specimens from different geographical origins.[52] The same is true for kaempferol[53] and genistein.[54] Furthermore, various triterpene glycosides and their aglycones were tested in binding assays for their affinity to estrogen receptor beta (ER-β), but no notable binding activity was detected.[55,56] While phenolic substances (e.g., cinnamic acid esters) were originally characterized in Asian *Cimicifuga* species, they have meanwhile also been described for *C. racemosa*.[57,58]

In early research, a binding capacity of the constituents of a methanolic black cohosh extract to estrogen receptors (ERs) was elucidated.[51,59] This, together with the lutein-

Continues on page 12

Table 1. Clinical Trials with Black Cohosh for Treatment of Menopausal Symptoms

Publication	Study Design	Interventions	Outcome
Pethö, 1987[95]	Open study, N=50, change in therapy (pre-treatment estrogen), age $\bar{x}$=49 years	Dry extract,[a] 2x2 tablets daily, for six months	Significant decrease of Kupperman-Index (KI) from 17.6 to 9.2 after six months; no AEs
Stoll, 1987[62]	Double-blind, randomized, placebo- and reference-controlled study, N=80, age 45-58 years	Three groups: [1] Dry extract,[a] 2x2 tablets; [2] conjugated estrogen; or [3] placebo, for 12 weeks	Superiority of *Cimicifuga racemosa* (CR) compared to placebo; KI, Hamilton Anxiety (HAMA), vaginal cytology significantly improved; estrogen dose too low to yield effect against placebo; three AEs (weight gain)
Lehmann-Willenbrock, 1988[96]	Open, controlled, randomized study, N=60 hysterectomized women, with at least one remaining ovary, age <40 years	Four treatment groups: [1] Dry extract,[a] 2x2 tablets; [2] conjugated estrogen 1.25 mg per day; [3] estriol 1 mg per day; or [4] estrogen/progestogen combination, for six months	Significant decrease of KI in all groups; no influence on luteinizing hormone (LH) or follicle stimulating hormone (FSH); no AEs
Georgiev & Jordanova, 1996[97]	Open uncontrolled study, N=50 postmenopausal women	No data on medication; six-month duration	Decrease of KI and HAMA; no change in endometrium thickness
Mielnik, 1996[98]	Open uncontrolled study, N=34 postmenopausal women	No data on medication, for six months	Clinically relevant decrease of KI from >20 to <10 after one month
Nesselhut & Liske, 1999[72]	Non-interventional study, N=28, postmenopausal women, age $\bar{x}$=56.4 years	Dry extract,[a] tablets corresponding to 136 mg herbal substance per day, for 12 weeks	Clinically relevant decrease of KI after one month; no influence on LH, FSH, or prolactin; no hormonal effects; no increase in endometrium thickness; no AEs
Liske et al., 2002[75]	Randomized, double-blind, parallel group, N=152 (76/76), peri-and postmenopausal women, age $\bar{x}$=49.7/50.2 years	Dry extract,[a] one tablet, equivalent to 39 mg herbal substance per day; one tablet equivalent to 127.3 mg herbal substance per day, for 12-24 weeks	Significant decrease of KI in both groups; no differences in Self-Depression Scale (SDS), Clinical Global Impression (CGI) scale, or vaginal cytology between treatment groups; no changes in gyn. hormones; no serious AEs
Wuttke et al., 2003,[99] 2006[87]	Randomized, double-blind, placebo- and comparator-controlled, multicenter, N=95 (62 included), age $\bar{x}$=52.25-54.05 years	Three groups: [1] Dry extract,[b] 2x2.8 mg per tablet, equivalent to 40 mg herbal substance per day; [2] conjugated estrogens 0.6 mg per day; [3] or placebo, for 12 weeks	Comparable improvement of Menopause Rating Scale (MRS I, performed by physician) total score under both treatments and superiority vs. placebo, but statistically just below significance; no serious AEs
Osmers et al., 2005[100]	Randomized, double-blind, placebo-controlled, multicenter, N=304 postmenopausal women (153/151), age $\bar{x}$=53/54 years	Dry extract,[a] 2x2.5 mg per tablet, equivalent to 40 mg herbal substance per day; or placebo, for 12 weeks	Significant improvement of the total score of MRS I; no serious AEs
Nappi et al., 2005[78]	Randomized, comparator-controlled, N=64 menopausal women (32/32), age $\bar{x}$=50.5/50.9 years	Dry extract,[a] 2x2.5 mg per tablet, equivalent to 40 mg herbal substance per day; transdermal estradiol (25 µg + progesterone 10 mg), for 12 weeks	Identical improvement under both treatments; no changes in gyn. hormones, lipids, liver function, or endometrium thickness; no AEs
Schmidt et al., 2005[101]	Observational study, N=502, age $\bar{x}$=56 years	Dry extract,[a] 2x2.5 mg per tablet, equivalent to 40 mg herbal substance per day, for 12 weeks	Improvement in KI
Vermes et al., 2005[102]	Observational study, N=2,016	Dry extract,[a] 2x2.5 mg per tablet, equivalent to 40 mg herbal substance per day, for 12 weeks	Improvement in KI
Frei-Kleiner et al., 2005[103]	Randomized, double-blind, placebo- controlled, multicenter, N=122 peri- and postmenopausal women (81/41), age $\bar{x}$=52.2/52.5 years	Dry extract,[c] one 6.5-mg capsule, equivalent to 40 mg herbal substance per day; or placebo, for 12 weeks	No significant difference of mean decrease in weekly weighted score of hot flashes (37% CR group, 30% placebo group) and in KI (26% CR group, 17% placebo group); significant difference in subgroup (perimenopausal patients with KI≥20); no serious AEs
Brattström, 2005,[104] Kaiser et al., 2008,[105] Schellenberg et al., 2012[106]	Randomized, double-blind, placebo-controlled, three-armed, N=180 pre-, early-, and postmenopausal patients, age $\bar{x}$=51.7 years, 166 patients included (57/55/54)	Dry extract,[c] 6.5 or 13 mg per two tablets once daily (double-dummy, parallel group design), equivalent to 40 mg (low dose) or 80 mg (high dose) herbal substance; or placebo, for 12 weeks	Significant decrease of KI in both groups (low and high dose) compared to placebo; significant decrease of KI in high-dose group compared to low-dose group; no serious AEs
Rauš et al., 2006[81]	Open label, non-comparative, prospective, multicenter; N=400 postmenopausal patients, 375 patients completed, age $\bar{x}$=56.38 years	Dry extract,[b] two 2.8-mg tablets, equivalent to 40 mg herbal substance per day, for 52 weeks	No case of hyperplasia or more serious adverse endometrial outcome; number of hot flashes decreased

Table 1, continued. Clinical Trials with Black Cohosh for Treatment of Menopausal Symptoms

Publication	Study Design	Interventions	Outcome
Newton et al., 2006,[107] Reed et al., 2008[108]	Randomized, double-blind, placebo-controlled, five-armed study, N=351 late- or postmenopausal women, age $\bar{x}$=52.2 years	Six groups: [1] Dry extract,[d] DER not specified, ethanol 70%; [2] 160 mg per day standardized to 2.5% triterpene glycosides; [3] multi-botanical with CR 200 mg per day; [4] multi-botanical plus soy diet; [5] Conjugated equine estrogens 0.625 mg per day with or without medroxyprogesterone acetate; or [6] placebo, for 12 months	No difference in vasomotor symptoms between the herbal interventions and placebo after three, six, and 12 months
Briese et al., 2007[109]	Non-interventional study, comparator-controlled, multicenter, N=6,141 (3,027/3,114), age $\bar{x}$=52.7 years	Dry extract,[a] 2x2.5 mg per tablet, equivalent to 40 mg herbal substance per day; combination preparation containing 3.75 mg of the above plus 70 mg of an ethanolic extract from 245-350 mg St. John's wort (*Hypericum perforatum*, Hypericaceae) two tablets, equivalent to 60-120 mg herbal substance per day, for 24 weeks	Significant decrease in MRS I in both groups in all items; AE rate 0.16%
Lopatka et al., 2007[110]	Observational study, N=584 peri- and postmenopausal patients with menopausal complaints, 541 completed, age $\bar{x}$=53.2 years	Dry extract,[c] one 6.5-mg tablet, equivalent to 40 mg herbal substance per day, for 16 weeks	Improvement in MRS II (performed by patient) score
Bai et al., 2007[111]	Randomized, double-blind, multicenter, comparator-controlled study, N=244 postmenopausal patients, age $\bar{x}$=50.9/51.8 years	Dry extract,[a] two 2.5-mg tablets, equivalent to 40 mg herbal substance per day; 2.5 mg tibolone, one tablet per day, for 12 weeks	Significant reduction of KI in both groups; significantly lower incidence of AEs in CR group compared to tibolone group
Oktem et al., 2007[112]	Prospective, randomized, open, comparator-controlled study, N=120 (60/60) menopausal or postmenopausal patients, age $\bar{x}$=52.7/53.7 years	*Cimicifuga* extract, DER and solvent not specified,[e] 40 mg per day; fluoxetine 20 mg per day, for six months	Improvement of KI in CR group, improvement of Beck Depression Inventory in the fluoxetine group
Geller et al., 2009[113]	Randomized, double-blind, placebo-controlled, four-armed study, N=89 peri- or postmenopausal patients with hot flashes and night sweats, age $\bar{x}$=53 years	Four groups: [1] Dry extract,[d] DER 20:1, ethanol 75%, 128 mg per day standardized to 7.27 mg triterpene glycosides; [2] red clover; [3] conjugated equine estrogens 0.625 mg per day with 2.5 mg medroxyprogesterone acetate; or [4] placebo, for 12 months	No difference in vasomotor symptoms between the herbal interventions; no serious AEs
Amsterdam et al., 2009[114]	Randomized, double-blind, placebo-controlled study of 50 (25/25) women with anxiety disorder due to menopause, age $\bar{x}$>40 years	Dry extract,[d] unspecified, 64mg (two capsules) daily or placebo for two weeks; black cohosh dose then gradually increased to four capsules per day for the remaining 10 weeks	No statistically significant anxiolytic effect vs. placebo
Li et al., 2011[115]	Placebo-controlled study, N=77 (45/32) with FSH>40 U/l and 17β-estradiol<20 pg/mL, KI≥17, age $\bar{x}$=50.4/51 years	Dry extract,[a] two 2.5-mg tablets, equivalent to 40 mg herbal substance per day; or placebo, for 12 weeks	Improvement of KI, no changes in FSH, LH, 17β-estradiol, lipid profile, liver function, endometrial thickness and vaginal maturation index (VMI)
Drewe et al. 2013[116]	Observational study, N=442 patients with menopausal complaints, age $\bar{x}$=52.3 years	Dry extract,[c] one 13-mg tablet, equivalent to 80 mg herbal substance per day for 12 weeks, then continuation for another six months with either the same or a half dose	Improvement in KI, especially in high-dose group
Mohammad-Alizadeh-Charandabi et al., 2013,[117] Shahnazi et al., 2013[118]	Randomized, double-blind, placebo-controlled study, N=84 (42/42) postmenopausal women with Greene Climacteric Scale (GCS) scores of 15 to 42, age $\bar{x}$=51.5 years	6.5 mg dry extract[f] per day, DER and extraction solvent not specified, standardized to 0.12-0.18 mg 27-deoxyactein; or placbo, for eight weeks	GCS scores significantly improved; no AEs

[a] Remifemin (Schaper & Brümmer; Salzgitter-Ringelheim, Germany); DER 6-11:1, propan-2-ol 40% (V/V)
[b] Klimadynon (Bionorica; Neumarkt, Germany); DER 5-10:1, ethanol 58% (V/V)
[c] Cimidona (Zeller; Romanshorn, Switzerland); DER 4.5-8.5:1, ethanol 60% (V/V)
[d] Extract composition does not match any known product; developed for study by the University of Illinois at Chicago (UIC)/National Institutes of Health (NIH) Center for Botanical Dietary Supplements Research
[e] Remixin (Mikro-Gen; Istanbul, Turkey)
[f] Cimifugol (Goldaru; Esfahan, Iran)

izing hormone (LH)-suppression observed in clinical studies[60] and changes in vaginal cytology attributed to administration of black cohosh rhizome extracts,[61,62] suggested efficacy due to an estrogen-like mode of action.[63,64] The question of possible estrogenic agonist effects is of central importance for product safety. While phytoestrogens in soy (*Glycine max*, Fabaceae) and red clover (*Trifolium pratense*, Fabaceae) support stimulation (e.g., of cell proliferation) by activating ERs in the estrogen-free system, black cohosh does not show a corresponding intrinsic effect.[65]


Black cohosh *Actaea racemosa*
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Various research groups have presented data that do not support estrogenic activity of black cohosh.[66-71] The organ specificity of estrogenic or antiestrogenic activity is now explained by the different, tissue-dependent occurrence of the two ER isoforms (ER-α and ER-β) as well as evidence of additional organ-specific coactivators and repressors.[70] The use of phytoestrogens in patients with breast cancer is associated with risks, as isoflavones may develop hormone-like effects (e.g., proliferation at the endometrium and breast tissue of menopausal women). However, in numerous clinical investigations, it was shown that Remifemin® (Schaper & Brümmer; Salzgitter-Ringelheim, Germany; DER 6-11:1, propan-2-ol 40% [V/V]), an isopropanolic extract of black cohosh, did not influence the mean values of LH, follicle stimulating hormone (FSH), prolactin, estradiol, or sex hormone binding globulin (SHBG), nor did vaginal cytology show any indications of systemic estrogen activity. Also, no increase in endometrial thickness was observed, which could be interpreted in terms of a proliferative stimulation of the endometrium.[69,72-85] Similar results were obtained with other extracts of black cohosh.[86,87]

Constituents of black cohosh could have a pharmacological effect in the central nervous system (CNS), mediated via alterations in opioid receptor activity. These areas of the CNS are also responsible for mediating the primary effects of estrogens.[88-90] Furthermore, the actions of black cohosh can be explained by the concomitant presence of ER-modulated but tissue-selective mixed agonistic/antagonistic behavior, and by its CNS-active, neutrotransmitter-modulated pathways.[67,91] There appears to be CNS activity, which is thought to have favorable therapeutic effects on menopausal symptoms, as well as positive effects on breast cancer cells and the endometrium through selective estrogen receptor modulation (SERM).[67,72-73]

Recent reviews summarize the existing knowledge and conclude that the exact modes of action of black cohosh remain unknown.[92,93] This would partially explain the inconsistent results of numerous preclinical and clinical investigations. On the other hand, the most recent review suggests reliable efficacy and an overall excellent safety profile based on an assessment of 11,073 patients receiving black cohosh products (93% of which were Remifemin) in 28 clinical trials published between 2000 and 2015.[94] Table 1 presents a summary of relevant clinical investigations affecting menopausal symptoms.

ADULTERATION

Adulteration of black cohosh is a serious concern that can have potential impacts on human health and safety as well as on ecosystems. Types of adulteration include unintentional (e.g., wild collection of look-alike species occurring in the same habitat) and intentional (e.g., substitution with Asian species of *Actaea,* which are considerably lower in cost than genuine black cohosh), the latter being more common. Known economic adulterants include *Actaea cimicifuga* (syn. *Cimicifuga foetida*), *A. dahurica* (syn. *C. dahurica*), *A. heracleifolia* (syn. *C. heracleifolia*), *A. simplex* (syn. *C. simplex*), *A. brachycarpa* (syn. *C. brachycarpa*), and possibly *Serratula chinensis* (Asteraceae). North American *Actaea* species that grow in the same areas as black cohosh, including *A. pachypoda*, *A. rubra*, and *A. podocarpa*, may also adulterate the supply.[119] In response, *HerbalGram* issue 98 (2013) included a comprehensive review by Steven Foster of black cohosh adulteration,[120] as the first in a series of black cohosh educational documents of the Botanical Adulterants Prevention Program (BAPP), led by the American Botanical Council (ABC), the American Herbal Pharmacopoeia (AHP), and the National Center for Natural Products Research (NCNPR) at the University of Mississippi. BAPP

published a black cohosh laboratory guidance document by Stefan Gafner, PhD, ABC's chief science officer, in 2015[121] and a botanical adulterants prevention bulletin, also by Gafner, in 2016.[119]

FUTURE OUTLOOK

In 2002, a proposal was made by the US Fish and Wildlife Service (USFWS) to consider including black cohosh in Appendix II of the Convention on International Trade in Endangered Species (CITES). Appendix II lists species that are not currently threatened with extinction but that may become so unless trade is closely controlled. According to the USFWS, the primary threats to black cohosh at that time were habitat loss and over-collection due, in part, to increasing domestic and international demand, with much of the harvest exported to Europe and Australia. Most black cohosh is wild-collected in the eastern United States, impacting tens of millions of individual plants per year, and it is cultivated only on a small scale. The USFWS also stated that "unauthorized collection in National Forests is reported to be extensive, and incidents of poaching from National Parks have been documented in recent years." Nonetheless, the USFWS notified the public in April 2002 that the United States did not intend to seek an Appendix II listing for black cohosh, but went on to state that in order to control illegal trade and generate additional trade data, it intended to review and consider listing US native species of the genus *Cimicifuga* in CITES Appendix III.[122] Appendix III is a list of species included at the request of a Party (member country) that already regulates trade in the species and that needs the cooperation of other countries to prevent unsustainable or illegal exploitation.

The NatureServe global conservation status rank for black cohosh is G4 (Apparently Secure), meaning it is uncommon but not rare with some cause for long-term concern due to declines or other factors. While NatureServe assigns a national conservation status of N4 (Apparently Secure) in the United States, the status for Canada is N2 (Imperiled), meaning it is at high risk of extinction or elimination due to a very restricted range, very few populations, steep declines, or other factors.[2] On the state level, other organizations list the species as endangered in Illinois and Massachusetts.[8] The nonprofit organization United Plant Savers places black cohosh on its "Species At-Risk" list.[123]

In their Appalachian plant monograph, Pengelly and Bennett (2012) caution that as clinical studies continue to strengthen the evidence of efficacy and safety for black cohosh, this inevitably puts more pressure on the raw material supply, which is still, for the most part, wild-collected. They conclude that sustainable wild harvesting is possible, but research thus far does not support it. Therefore, it is suggested that research funding should target experimental cultivation trials in both field and wild-simulated settings.[8] In the meantime, there is now certified organic black cohosh coming to market that conforms to the USDA organic wild-crop harvesting practice standard as well as some cultivation taking place on certified organic farms.[7] HG

—Josef Brinckmann and Thomas Brendler

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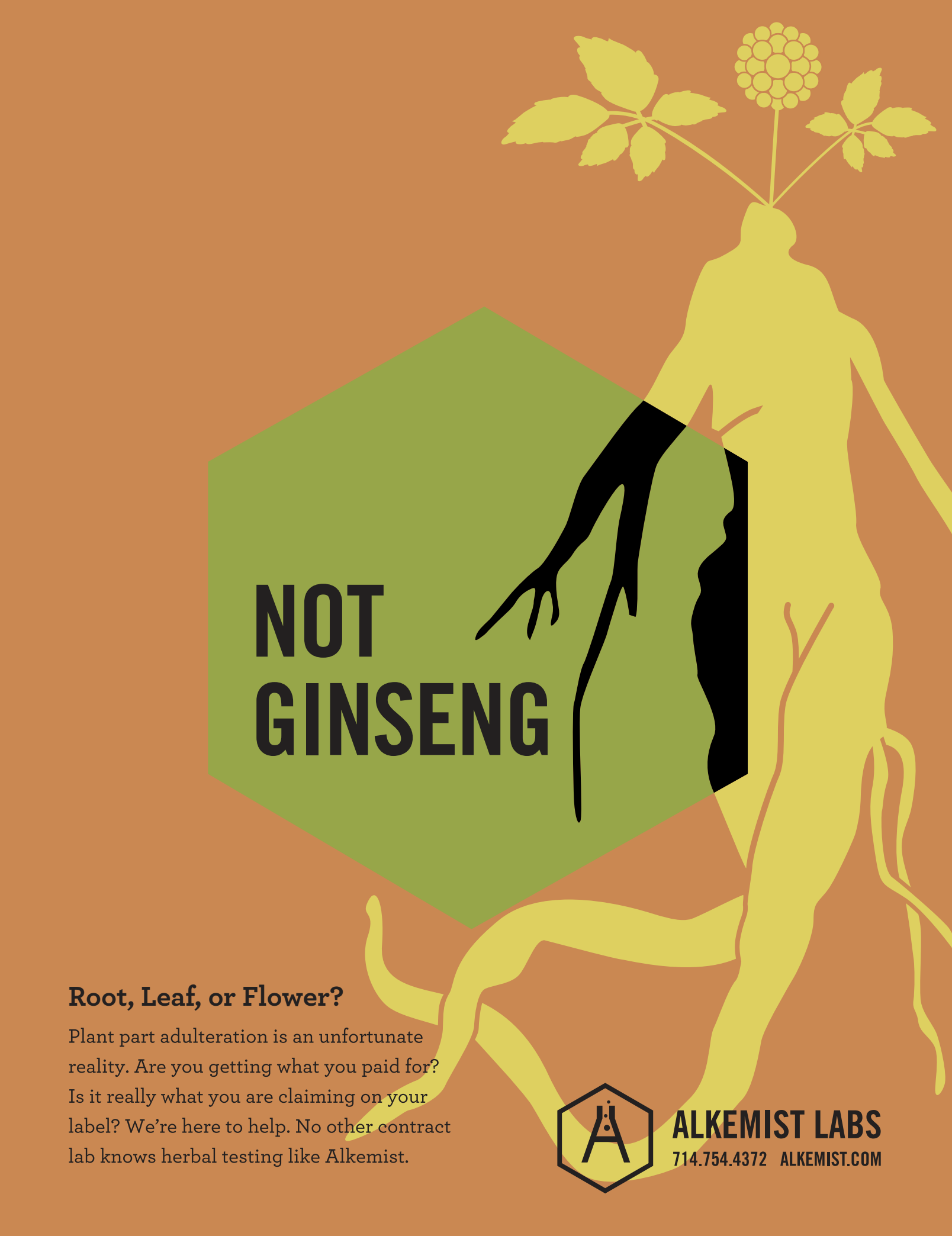

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Employee Profile: Caroline Caswell

Michigan native Caroline Caswell joined the American Botanical Council (ABC) staff in April 2016. Initially, she worked 10 hours a week in the gardens that surround the organization's 2.5-acre historic Case Mill Homestead. By November 2017, her responsibilities had grown so much that she was hired full time as education assistant, which still includes garden tasks. However, like most employees at ABC, Caswell oversees a variety of duties: maintaining ABC's literature database, coordinating ABC's volunteer program, and assisting the membership and accounting departments, in addition to her main responsibilities in ABC's education department.

Caswell came to ABC with an extensive background in gardening and herbal medicine. Dissatisfied with conventional treatments for a chronic illness in her early teens, Caswell began to research alternative therapies. "I learned how to grow my own food and never looked back," she explained. "I began dabbling in teas, making my own remedies, understanding what stress did to my body during college, and ultimately had to live a very different lifestyle than my peers. Falling in love with the magic of growing food kept my curiosity spiked." Caswell shaped her own course of study at Michigan State University to focus on her intersecting interests in plants, art, and social justice, and she completed a degree in Arts and Humanities with specializations in studio art, art history, and ecology. After graduation, she sought a respite from harsh winters and relocated to Austin, Texas.

In Austin, Caswell attended the Wildflower School of Botanical Medicine on the clinical herbalist track and knew she had found her calling. "I dived deep into the studies and fell in love with hundreds more plants," she said. "I now teach for the school and love to learn from each of my students, and the plants, of course. They are our biggest teachers." Caswell has since started her own clinical practice and line of herbal products, in addition to her full-time tasks at ABC, and teaches herbal medicine classes around the city. "Even though it means I work a lot," she added, "it truly feels like my mission to continue to do so."

ABC Special Projects Director Gayle Engels has welcomed Caswell and her knowledge of plants to the education team. "I know that everyone is as pleased as I am to have Caroline here at ABC full time," said Engels. "Not only is she helping the organization make progress on some major projects, but she is a pleasure to work with and a truly kind and generous person. Another plant person with Caroline's commitment is exactly what ABC's education department needed."

In her work, Caswell emphasizes the importance of an open connection between people and plants. "My philosophy focuses on warm and welcoming community-based wellness," she explained. "Herbal medicine is the medicine of the people. It is meant to be passed down, accessible, and incorporated into the everyday. Accessibility is central to what and how I teach."

Her favorite moments on the job come from introducing visitors to the ABC grounds and expanding their knowledge about healing plants: what they look like, how to cultivate them, and how to use them. "The folks who visit meet long-time plant allies for the first time or see a new specimen. 'Oh, so that's what ashwagandha [*Withania somnifera*, Solanaceae] looks like?' Interacting with the live plants will make you appreciate the tincture or supplement you buy in a bottle."

"ABC is not your everyday place," Caswell concluded. "Our gardens are a premier classroom. Much labor and love is put into them, and we have hundreds of species from all over the world. It is magic we are cultivating, and I want people to see that."

Caroline Caswell.
Photo courtesy of Caroline

As ABC grows, so, too, have Caswell's duties. While she treasures her time spent with ABC's themed gardens and greenhouse, Caswell has been assigned another project: the organization and cataloging of ABC's research library. She referred to the library as a "loving work in progress" and expressed her excitement to work with both well-known and more obscure herbal texts.

"ABC is not your everyday place," Caswell concluded. "Our gardens are a premier classroom. Much labor and love is put into them, and we have hundreds of species from all over the world. It is magic we are cultivating, and I want people to see that." HG

—Hannah Bauman

ABC's Gayle Engels to Receive HSA's Inaugural Award for Excellence in Herbal Education

The American Botanical Council's (ABC's) Special Projects Director Gayle Engels will receive The Herb Society of America's (HSA's) inaugural Madalene Hill Award for Excellence in Herbal Education at the HSA's Educational Conference and Annual Meeting of Members in Madison, Wisconsin, in June 2019. According to the HSA, the Hill Award honors those who "have a passion for promoting the knowledge, 'use and delight' of herbs through educational activities" and "show a great zeal for sharing their passion for herbs with the public."[1] The award is named in honor of the "Grand Dame of Herbs" Madalene Hill, who died in 2009 at the age of 95.[2]

Engels helps manage ABC's educational efforts, garden development, and other projects. Her work with the HerbDay Coalition and active membership with the HSA allow Engels to share her love of botanicals and their beneficial qualities with students, herbalists, and the general public. Her deep knowledge of herbs and medicinal and aromatic plants has expanded with her duties as the director for ABC's HerbMedPro database. She also has co-authored more than 30 herb profiles for *HerbalGram*. Through these efforts, Engels has immersed herself in scientific and clinical research, traditional uses, sustainability issues, and distribution of hundreds of plants.

For Engels, pursuing the role of educator came naturally. "I have always loved learning," she wrote (email, December 4, 2018). "As a child, as much as I loved vacation, I didn't mind when it ended so I could go back to school. From an early age, everything that interested me, I pursued resolutely…. I decided to major in secondary education because of my love of learning and because I loved the light in a person's eyes when they learned something that mattered to them."

Her mother's peppermint (*Mentha* × *piperita*, Lamiaceae) tea and her aunt's gifts of chamomile (*Matricaria chamomilla* syn. *M. recutita*, Asteraceae) inspired Engels' love of botany and herbs at an early age. Before working at ABC, Engels owned a small landscaping business and worked at several plant nurseries in Austin, Texas.

In 1995, Engels joined the staff of ABC. Her new position allowed her to employ both her knowledge of plants and her love of teaching. "I knew that [ABC] would provide me the opportunity to grow and learn and teach. From May 8, 1995, forward I've been able to play with plants and books and databases and share what I continue to learn with pretty much everyone with whom I come in contact," Engels wrote. "Working with the interns, introducing them to the wonders of the plants, seeing them light up when you find the right aspect of herbs to ignite their interest, and sometimes passion, is ABC's mission in action for me."

Gayle Engels in the ABC gardens.
Photo courtesy of Gayle Engels.

ABC Founder and Executive Director Mark Blumenthal, a past Honorary President of HSA, endorsed Engels' nomination for the award in a letter dated August 29, 2018, to Henry Flowers, a lifetime member of HSA and past chair of the HSA's Pioneer Unit of Central Texas. Blumenthal wrote: "My positive opinion of [Engels] and her strong dedication to the world of herbs and medicinal plants has continued to grow to a point where I believe it can go no further; that is, my regard and admiration for her life's profound commitment to the world of herbs cannot be any stronger or better."

The award's namesake, Madalene Hill, was an internationally recognized herbalist and author.[2] Born and raised in Texas, she ran a successful herb business and restaurant, Hilltop Herb Farm, in Cleveland, Texas, with her husband Jim. Hill eventually joined the Round Top Festival Institute

Left: Madalene Hill's hands ©2019 Susan Belsinger.
Right: Engels aspires to have hands that tell gardening stories like Hill's.

in Round Top, Texas, as curator of the Susan Clayton McAshan Herb Gardens when her daughter, Gwen Barclay, became the Institute's food services manager. Through Hill's guidance and leadership, the Institute expanded its gardens and outreach efforts, and Hill oversaw special programs throughout the year to introduce visitors to the culinary and medicinal uses of herbs. These programs included guided garden tours, herb-inspired luncheons, and workshops on growing herbs and designing and cooking with herbs. In addition, Hill served as the president of HSA from 1986 to 1988.

Gayle Engels with Madalene Hill.

Hill received numerous recognitions for her work: She was awarded the HSA's Helen de Conway Little Medal of Honor in 1978, Nancy Putnam Howard Award for Excellence in Horticulture in 1997, Gertrude B. Foster Award for Excellence in Herbal Literature (shared with Barclay) in 2005 for their book *Southern Herb Growing* (Shearer Publishing, 1987), and the Golden Sage Award, which recognized Hill's 50 years of membership, in 2009. She also received the American Horticultural Society's Catherine H. Sweeney Award in 2006 for extraordinary and dedicated philanthropic efforts in the field of horticulture. Seven herbs have been named in her honor. Now, an award will bear her name and honor those who follow in her footsteps of herbal education and outreach.

Flowers, who curated the McAshan Gardens for 16 years and worked with Hill for seven, initially proposed the idea for the Madalene Hill Award in the summer of 2017. "She was a fabulous mentor," he wrote (email, December 4, 2018). "Her love of what she called 'these little plants' was very deep and even though she had no formal education beyond high school, her inquisitiveness drove her to constantly be researching, growing, using, and experimenting with herbs." The HSA board unanimously approved the new award in the fall of 2017.

"When Madalene passed away, the world of herbs lost a great advocate," Flowers wrote. "[She was] always willing to share her knowledge with others, either for a large group of hundreds or in a one-on-one situation. I consider Madalene to have been a great educator in the field, even though she was never an educator in the formal sense. After Madalene's passing, I felt that it would be wonderful to honor her by having an award given by the Herb Society of America named for her. The HSA has many wonderful awards for a variety of purposes, but at the time had no award to honor someone specifically for their efforts in the area of herbal education."

Engels had a personal relationship with Hill, which makes the award all the more meaningful to her. "I benefitted greatly from knowing Madalene Hill," Engels wrote. "I spent as much time as possible with Madalene in the McAshan Gardens at Festival Hill, and many of the plants in ABC's gardens, such as the tamarind (*Tamarindus indica*, Fabaceae) and physic nut (*Jatropha multifida*, Euphorbiaceae), were gifts from the McAshan Gardens. Before long, Madalene began inviting me to speak at the Annual Herbal Forum held at the Festival Institute each March.

"Madalene was a teacher, a gardener, a mentor, an entrepreneur, a plantswoman, a premier repository of plant knowledge, and one of the most eager learners and most generous people I've had the pleasure of knowing," Engels added. "My favorite herbalists are the ones who, no matter how long they have been studying, admit that there is always more to learn and that each plant and person should be treated according to their individual needs."

Flowers considered many different candidates for the award, but "the one person that kept coming to the forefront was Gayle Engels," he wrote. "In my time as director of the Herbal Forum at Round Top, Gayle had presented wonderful lectures about the medicinal aspects of many herbs and had also presented wonderful demonstrations and workshops. Gayle is always thorough, backs her presentations with good research, and is able to make the subject understandable to a general audience of herb enthusiasts.

"Madalene Hill knew Gayle for many years and I know that she always thought highly of her," Flowers continued. "In making my nomination of Gayle for this award, I knew that Madalene would approve wholeheartedly." HG

—Hannah Bauman

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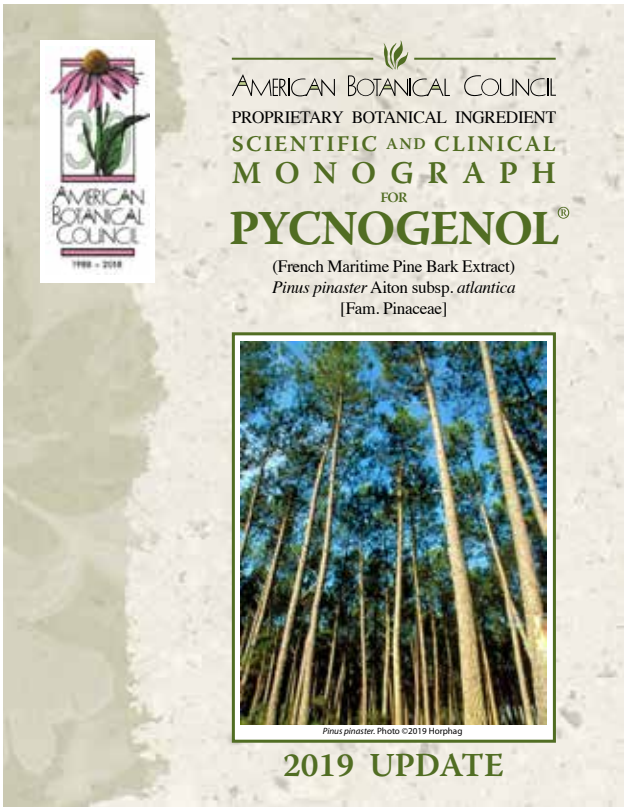
ABC Publishes Updated Monograph on French Maritime Pine Bark Extract Pycnogenol®

46-page monograph describes scientific research and human clinical trials that support various medicinal uses

The American Botanical Council (ABC) has published an updated ingredient-specific monograph that summarizes selected scientific and clinical studies of Pycnogenol, a patented dietary ingredient derived from French maritime pine (*Pinus pinaster* subsp. *atlantica*, Pinaceae) bark. ABC's original monograph on Pycnogenol was published in 2010.

The revised monograph summarizes 63 human clinical trials on Pycnogenol — 46 more than the original monograph. The studies evaluated the proprietary extract's potential benefits for numerous health conditions, including chronic venous insufficiency (improper leg vein function), thrombosis (formation or presence of clots in blood vessels), type 2 diabetes, and hypertension.



The evidence from the selected trials suggests that Pycnogenol may have a wide range of potential applications, including the ability to improve blood sugar control in patients with type 2 diabetes and improve endothelial function (e.g., the ability of blood vessels to widen through relaxation of the muscular wall of the vessels). Clinical trial data suggest that Pycnogenol may also help decrease edema formation (swelling) in the lower legs, benefit children with ADHD, be a useful adjunct therapy for patients with asthma, reduce pain associated with menstrual disorders, and improve subjective symptoms of osteoarthritis in the knee.

"Few proprietary botanical extracts have been subjected to human clinical trials in such a wide range of human health conditions," said Mark Blumenthal, founder and executive director of ABC. "We acknowledge Horphag Research, the producer of Pycnogenol, for its strong commitment to clinical research on its leading ingredient."

Horphag Research of Geneva, Switzerland, invests about $1.5 million annually in new scientific and clinical research on the extract.

According to Victor Ferrari**,** CEO of Horphag Research: "The new ABC monograph is the most comprehensive technical document on Pycnogenol to date. It will help tremendously in educating the industry and scientific audience and sets the foundation for all future developments and research to come. Horphag Research is committed to continue the path of evidence-based science and innovation."

The monograph is published in three parts: a clinical overview (i.e., executive summary) that contains condensed information from the larger monograph, a consumer/patient information sheet with essential information for the responsible use of the product, and the full monograph that describes scientific and clinical research on Pycnogenol. Each of these parts is accessible separately on the ABC website.

The full monograph contains an overview of Pycnogenol's production and chemistry, uses of the product, dosage information, descriptions of the product's pharmacology and mechanisms of action, safety data, and summaries of selected clinical trials. A 13-page table includes synopses of the clinical trials profiled within the monograph's text, plus summaries of several additional studies. The monograph also includes patent information and describes how Pycnogenol is regulated in 10 countries and regions around the world.

Horphag Research has studied the extract extensively over the past 49 years to assure the safety and efficacy of Pycnogenol as an ingredient in dietary supplements and conventional foods. According to the company, more than 100 clinical trials and 400 scientific studies and review articles have been published on the extract. Horphag Research earned the Frost & Sullivan North American Health Ingredients Excellence in Research of the Year Award for

2008, and ABC presented the company with the Varro E. Tyler Commercial Investment in Phytomedicinal Research Award in 2012.

ABC's ingredient-specific monograph on Pycnogenol was written by toxicologist Heather S. Oliff, PhD, and peer reviewed by scientific and medical experts for its accuracy. "The Pycnogenol monograph is a useful compendium because it is a very thorough and unbiased review of the scientific literature," Oliff said.

ABC emphasizes that the publication of the Pycnogenol monograph is not an endorsement or recommendation of the ingredient or the manufacturer. "ABC has had a long history of documenting specific herbal products and ingredients that have been clinically tested," said Blumenthal. "As part of our nonprofit research and educational mission, we believe it is in the public interest to identify human clinical research conducted on natural plant-based products and ingredients that the scientific literature suggests are safe and beneficial."

ABC's Pycnogenol monograph is the fifth in a series of product- or ingredient-specific monographs that the organization has published. It was produced under an educational grant from Horphag Research to ABC. The organization has plans to produce additional monographs concerning specific researched commercial products and ingredients.

About Horphag Research

Horphag Research Ltd., founded in 1925 and based in Geneva, Switzerland, is the exclusive worldwide supplier of Pycnogenol. The company leads the world in Pycnogenol research, and new applications for Pycnogenol are explored every year. Pycnogenol is available in more than 700 dietary supplements, multivitamins, and health products worldwide. Pycnogenol is a registered trademark of Horphag Research, and its applications are protected by US and international patents. Horphag Research USA Inc., based in Hoboken, New Jersey, is the exclusive North American raw material supplier of Pycnogenol. More information about Pycnogenol is available at the company's website: www.pycnogenol.com. HG

—ABC Staff

Pine *Pinus pinaster*
Photo ©2019 Steven Foster

American Botanical Council: 2018 Year in Review

In 2018, the American Botanical Council (ABC) celebrated many milestones and launched new projects to advance its nonprofit mission to educate the public and other stakeholders about diverse topics related to medicinal plants and other beneficial botanicals. As a recognized leader in the field of responsible, science-based herbal medicine education, ABC's efforts in 2018 — including the launch of its newest partnership, the Sustainable Herbs Program — impacted community members both locally and internationally.

ABC's educational services and platforms reach individuals in more than 80 countries. These include numerous unique publications, an information-rich and constantly growing website, online databases, social media, lectures, consulting and research services, media education outreach, an online bookstore, herbal demonstration gardens, educational events, and an internship program for graduating pharmacy and dietetic students. The organization's activities serve those in the herbal community, including consumers, health care practitioners, academic researchers, educators, professionals from all segments of the natural products and health industries, government employees, the media, and more.

ABC Anniversaries

On November 1, 2018, ABC celebrated its 30th anniversary as a nonprofit organization. ABC is deeply grateful to the many individuals, companies, and organizations that helped make this possible through their support throughout the years.

ABC plans to continue the celebration of its 30th anniversary throughout 2019 with special announcements and opportunities for the public to show its support. ABC board, staff, and supporters already are making plans for how to advance ABC's unique and essential nonprofit educational mission for the next 30 years.

Other ABC milestones in 2018 included the 35th anniversary of *HerbalGram*, the 25th anniversary of ABC's HerbClip program, and the publication of its 7,000th HerbClip summary/critique of clinical studies and related botanical science publications. In 2018, ABC also celebrated 20 years at its historic Case Mill Homestead in Austin, Texas.

New Projects, Programs, and Awards

The Sustainable Herbs Program (SHP) partnership was launched by ABC on November 1, 2018. This educational and inspirational program and its video-rich website (www.sustainableherbsprogram.com) focus on promoting a responsible, sustainable, and regenerative herb supply chain. It does this by creating and disseminating tools and resources for the international herb and medicinal plant communities, including those involved at every point along the herb supply chain.

The ABC-American Herbal Pharmacopoeia (AHP)-National Center for Natural Products Research (NCNPR) Botanical Adulterants Prevention Program (BAPP) had a stellar year in 2018. It published its 47th peer-reviewed document and released a draft of "Best Practices Standard Operating Procedure (SOP) for the Disposal or Destruction of Irreparably Defective Articles." This SOP draft provides boilerplate supply contract language to help ensure that, through appropriate industry self-regulation, the supply chain is rid of defective ingredients that are irreparable and not acceptable for consumer products. All of the BAPP's publications are freely available to the public after registration at www.botanicaladulterants.org. More information about the SOP can be accessed by contacting abc@herbalgram.org.

ABC awarded its inaugural Fredi Kronenberg Excellence in Botanicals for Women's Health Award to Tieraona Low Dog, MD. The award was named after long-time ABC Board of Trustee Member Fredi Kronenberg, PhD, who died in 2017. Kronenberg's distinguished professional life focused on the study of using medicinal plants and phytomedicines for women's health.

In 2018, it was also announced that Gayle Engels, ABC's special projects director, will receive The Herb Society of America's (HSA's) inaugural Madalene Hill Award for Excellence in Herbal Education. Engels, who has been with ABC since 1995, will receive the award because of her "passion for promoting the knowledge, 'use and delight' of herbs through educational activities."

New Adopt-an-Herb Program Participants

In 2018, the 63rd herb was adopted on ABC's HerbMedPro database through the ABC Adopt-an-Herb Program. The support of adopters helps ABC keep the records of adopted herbs up to date in its HerbMedPro database. The result is increased public awareness and access to reliable, science-based information on these and other herbs.

ABC recognized the following six adoptions in 2018: propolis, attributed to Friends of the Honey Bee; EpiCor® Fermentate by Embria Health Sciences; pomegranate (*Punica granatum*, Lythraceae) by Verdure Sciences; lemon balm (*Melissa officinalis*, Lamiaceae) by Four Elements, grape (*Vitis vinifera*, Vitaceae) by Natac, and saw palmetto (*Serenoa repens*, Arecaceae) by Valensa.

In 2018, ABC also:

- Published its 2017 US Herb Market Report, which showed an 8.5% increase in total herbal supplement retail sales from the previous year.
- Awarded six Botanical Excellence Awards to individuals and companies for their valuable contributions to the herbal and botanical community.
- Published four issues of *HerbalGram*, 12 issues of HerbalEGram, 51 issues of Herbal News & Events, 360 HerbClips, five Botanical Adulterants Prevention Bulletins, three Laboratory Guidance Documents, and three Botanical Adulterants Monitor newsletters.
- Issued 30 press releases and fielded more than 31 media requests. As a reliable third-party educational resource, ABC helps the media develop a more rational understanding and/or interpretation of scientific, regulatory, and market data.
- Trained six pharmacy and dietetic interns from sixth-year pharmacy school and graduate dietetic programs. Many of these interns were introduced to the science behind botanicals, herbal medicine, and various fruits, vegetables, culinary herbs, and spices for the first time for potential inclusion in their future practices.
- Hosted more than 700 visitors at its historic 2.5-acre headquarters throughout the year. These visitors included children, seniors, college students (including medical and nursing students), garden clubs, herbalists, health care providers, and other interested members of the local community. There was also a strong turnout at ABC's annual HerbDay celebration in May. HG

—ABC Staff

Adoptions by Afrigetics Botanicals and Natural Remedies Support ABC's Adopt-an-Herb Program

The American Botanical Council (ABC) recently announced the adoptions of two botanicals in its Adopt-an-Herb research and education program: the South African herb bulbine (*Bulbine natalensis*, Xanthorrhoeaceae) by Afrigetics Botanicals, a company that specializes in African herbal products; and licorice (*Glycyrrhiza* spp., Fabaceae) by Natural Remedies, an herbal products research and development company.

These adoptions support ABC's extensive HerbMedPro database, ensuring that this unique research and educational resource remains up to date for researchers, health professionals, industry members, students, consumers, and other members of the herbal and dietary supplements and natural medicine communities.

HerbMedPro is a comprehensive, interactive online database that provides access to important scientific and clinical research data on the uses and health effects of more than 265 herbs, spices, and medicinal plants.

Afrigetics Botanicals Adopts Bulbine

Afrigetics Botanicals' mission is to commercialize African medicinal plants. According to Steve Hurt, CEO and sales director of Afrigetics Botanicals, more than 3,000 medicinal plant species are used in southern Africa, but only a limited number of those, including rooibos (*Aspalathus linearis*, Fabaceae), devil's claw (*Harpagophytum* spp., Pedaliaceae), pelargonium (*Pelargonium sidoides*, Geraniaceae), and sceletium (*Sceletium tortuosum*, Aizoaceae), are used in products in the United States.

Hurt hopes the adoption of *B. natalensis* will help introduce the plant to the North American market and encourage additional scientific studies on its potential medicinal benefits. "In my opinion, as it appears to me from the trade shows I've been to and the people with whom I've spoken, ABC is the authority on herbs and herbal medicine in the United States," Hurt said. "So, we thought that ABC would be a good partner to work with." He added that *B. natalensis* may be a promising ingredient for bodybuilding and fitness enthusiasts because stem extracts of the plant have been shown to increase testosterone levels in animal models. Human studies are needed, however.

Stefan Gafner, PhD, ABC's chief science officer, said: "We are grateful to Afrigetics Botanicals for its adoption of *Bulbine natalensis*. The African continent has a rich history of medicinal plant use, and a large number of these plants are relatively unknown to the Western world. The adoption allows us to make the science behind *Bulbine natalensis* easily accessible and introduce this plant to a larger audience in the United States and elsewhere."

Bulbine *Bulbine natalensis* illustration
Image ©2019 Afrigetics Botanicals

About Bulbine

Bulbine natalensis is a perennial evergreen in the same plant family (Xanthorrhoeaceae) as aloe (*Aloe vera*). Like aloe, *B. natalensis* is a succulent. It has large, broad, pointed, fleshy, thornless, yellowish-green leaves that grow in a rosette and can bruise easily. It is a frost-tender plant (i.e., it often is damaged or killed by even minimal frost), but it is heat- and drought-tolerant. Elongated clusters of star-shaped yellow flowers usually appear in July or August on long, thin stems that are two to three times as long as the leaves.

This species is one of more than 50 South African *Bulbine* species. It is widely distributed in the eastern and northern parts of South Africa, though reportedly is most common in the dry valleys of Eastern Cape province. It often is found on cliff edges and in rocky areas with poor soil. Some sources consider *B. natalensis* and *B. latifolia* to be synonyms, but, according to *Medicinal Plants of South Africa* (Briza Publications, 2009), the latter is sometimes considered a separate species from Eastern Cape with dark green, firm leaves and dense flowers. Both species are used medicinally and often co-occur in Eastern Cape.

Bulbine natalensis is known locally as *ibhucu* (Zulu), *ingcelwane* (Xhosa), and *rooiwortel* (Afrikaans). The genus name *Bulbine* is derived from the Greek for "bulb," even though most *Bulbine* species reportedly do not have a bulb. *Bulbine* species, including *B. natalensis*, can be distinguished from other similar plants by their floral characteristics, specifically their hairy stamens that bear the anthers.

The medicinal uses of *Bulbine* species, including *B. natalensis*, generally resemble those of aloe. Traditionally, the leaf gel of *B. natalensis* has been used to treat wounds, burns, rashes, itches, ringworm, and cracked lips. In addition, root preparations have been used in local healing traditions for vomiting, diarrhea, convulsions, venereal diseases, diabetes, and rheumatism.

In an animal study, male rats that were given an aqueous extract of *B. natalensis* stem exhibited increased testosterone levels, but more evidence is needed to support the traditional use of the plant to treat male sexual dysfunction. In a separate study on pigs, wounds that were treated with either *B. natalensis* or *B. frutescens* leaf gels improved significantly compared to untreated wounds. In a third study on rats, an extract of *B. natalensis* leaves demonstrated antiplatelet aggregation activity.

Licorice *Glycyrrhiza gabra*
Photo ©2019 Steven Foster

About Afrigetics Botanicals

Established in 2008 and headquartered in George, Western Cape, South Africa, Afrigetics Botanicals claims to be "one of the leading exporters of Southern African medicinal herbs, teas, oils and foods to the international wellness and pharmaceutical industries," according to its website. The company specializes in horticulture, African ethnopharmacology, agri-processing, and sustainable wild harvesting. It also believes that "the botanical resources of Africa may hold the key to the treatment of major medical and health ailments."

Afrigetics Botanicals produces AnaTest, a solvent-free, ultrasonically extracted powder of *B. natalensis* stem. The rural communities from which Afrigetics Botanicals obtains its supply of *B. natalensis* receive a profit share, in addition to payment for the plant material. According to Hurt, most of the supply of *B. natalensis* is wild-harvested under license and guidance of South African Nature Conservation, but the company also cultivates the species.

Natural Remedies Adopts Licorice

Natural Remedies CEO and Managing Director Anurag Agarwal said: "We are proud of being associated with the American Botanical Council for adopting licorice. Our brand, Gutgard®, is a clinically researched flavonoid-rich extract of licorice root and rhizome. This partnership stems from our core value of 'being useful,' as we want the world to recognize, through this adoption, the benefits of licorice in improving gut health. We are committed to unveiling the mystery of licorice with focused research which will ultimately strengthen the value offered by Gutgard to our customers."

Mark Blumenthal, ABC's founder and executive director, said: "On behalf of all of us here at ABC, we offer our profound thanks and gratitude to our good friends at Natural Remedies in Bengaluru for their adoption of licorice, a widely used medicinal plant with a vast array of traditional and modern therapeutic uses. Natural Remedies' adoption of licorice allows ABC to share up-to-date information on this ancient natural remedy with our members and the public."

About Licorice

Licorice species are perennial herbs native to the Mediterranean region, Asia Minor to Iran, and central to southern Russia, and are widely cultivated throughout Europe, the Middle East, and Asia. The root is the primary plant part used in medicinal preparations. Medicinal use of licorice has been documented as far back as 2100 BCE, and licorice root preparations have been used in traditional medicinal systems, including Ayurveda, Siddha, Unani, and traditional Chinese medicine. In modern times, licorice root has been studied for its gastrointestinal benefits, particularly for ulcers; upper respiratory tract infections; and anti-inflammatory actions that may help treat allergic reactions, rheumatism, arthritis, and other conditions.

The root of *G. glabra* has a long history of traditional therapeutic use for treating digestive issues. Glycyrrhizin (also called glycyrrhizic acid), a triterpene saponin from licorice, is one of the herb's well-known active constituents and the main sweet-tasting component.

Gutgard is an innovative, natural, clinically-researched bioactive preparation for gut health. It is different from deglycyrrhizinated licorice (DGL) with respect to chemistry and composition, the manufacturing process, mechanisms of action, and physicochemical properties. Most of the generic DGL-based extracts are byproducts of a chemical process used to separate glycyrrhizin from licorice.

Gutgard is standardized to contain 10% or more of total flavonoids (by weight) and 0.5% or less of glycyrrhizin to avoid potential undesirable side effects. More than 50 flavonoids have been identified in the extract, including isoflavans (e.g., glabridin), flavones (e.g., licoflavone A), flavanones (e.g., glabrol), chalcones (e.g., isoliquiritigenin), and isoflavones (e.g., formononetin).

Licorice flavonoids have been shown to have beneficial activities related to the digestive system. Gutgard has been shown to be beneficial in digestive issues and also in reducing the gastric load of *Helicobacter pylori*.

About Natural Remedies

Natural Remedies Pvt. Ltd. is a global, research-driven, botanical health care company based in Bengaluru, India, whose core competency lies in manufacturing standardized herbal extracts. According to the company, its mission is to harness nature and apply science for health and happiness. Natural Remedies' branded products are clinically substantiated and scientifically validated innovations. Known as a leader in standardized botanical extracts, Natural Remedies has contributed to the development of monographs on Indian botanicals in various international pharmacopeias. The company also has been a leading producer and global supplier of high-purity phytochemical reference standards for quality control of and research on Indian medicinal plants.

About Adopt-an-Herb and HerbMedPro

Afrigetics Botanicals and Natural Remedies are among the 58 US and international companies that have supported ABC's educational efforts to collect, organize, and disseminate reliable, traditional, and science-based information, including clinical studies, on herbs, medicinal plants, and other botanical- and fungal-based ingredients through the Adopt-an-Herb program. This program encourages companies, organizations, and individuals to "adopt" one or more specific herbs for inclusion and ongoing maintenance in the HerbMedPro database. To date, 64 herbs have been adopted.

Each adopted herb is continuously researched for new scientific articles and botanical, chemical, pharmacological, toxicological, and clinical studies, ensuring that its HerbMedPro record stays current and robust. Access to the studies is conveniently organized by publication type, with each study condensed to a one-sentence summary with a link to the study's official abstract on PubMed (the US National Library of Medicine's free-access database) or other publicly accessible database.

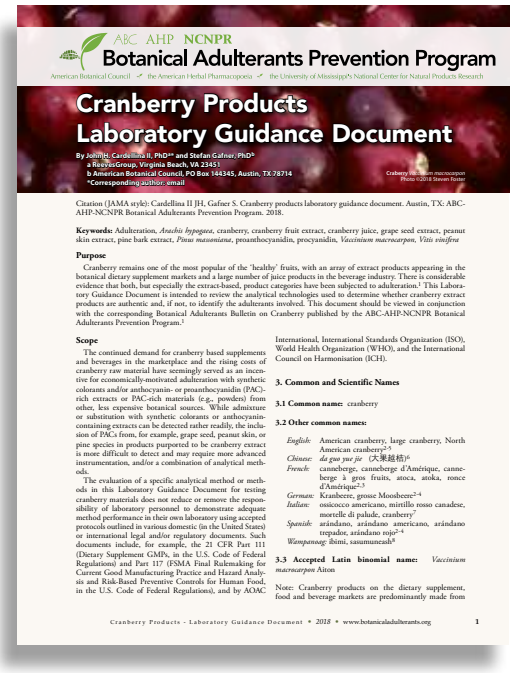
HerbMedPro is available to ABC members at the Academic level and higher. Its "sister" site, HerbMed, is available to the general public at no cost, with access to 25-30 herb records from the larger HerbMedPro database. In keeping with ABC's position as an independent research and education organization, herb adopters do not influence the scientific information that is compiled for their respective adopted herbs. HG

—ABC Staff

Botanical Adulterants Prevention Program Publishes Cranberry Laboratory Guidance Document

The ABC-AHP-NCNPR Botanical Adulterants Prevention Program (BAPP) recently announced the publication of a new Laboratory Guidance Document (LGD) on cranberry (*Vaccinium macrocarpon*, Ericaceae).

Cranberry-derived dietary supplements and beverages are widely used for the prevention and adjuvant treatment of recurrent urinary tract infections. In the United States, cranberry was the third top-selling botanical dietary supplement ingredient in US mainstream retail outlets (drug stores, grocery stores, etc.) in 2017, with sales of $68.12 million.


ABC AHP NCNPR
Botanical Adulterants Prevention Program
American Botanical Council ~ the American Herbal Pharmacopoeia ~ the University of Mississippi's National Center for Natural Products Research

Cranberry Products
Laboratory Guidance Document

By John H. Cardellina II, PhD[a]* and Stefan Gafner, PhD[b]
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Cranberry (*Vaccinium macrocarpon*)
Photo ©2018 Steven Foster

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Keywords: Adulteration, *Arachis hypogaea*, cranberry, cranberry fruit extract, cranberry juice, grape seed extract, peanut skin extract, pine bark extract, *Pinus massoniana*, proanthocyanidin, procyanidin, *Vaccinium macrocarpon*, *Vitis vinifera*

Purpose

Cranberry remains one of the most popular of the 'healthy' fruits, with an array of extract products appearing in the botanical dietary supplement markets and a large number of juice products in the beverage industry. There is considerable evidence that both, but especially the extract-based, product categories have been subjected to adulteration.[1] This Laboratory Guidance Document is intended to review the analytical technologies used to determine whether cranberry extract products are authentic and, if not, to identify the adulterants involved. This document should be viewed in conjunction with the corresponding Botanical Adulterants Bulletin on Cranberry published by the ABC-AHP-NCNPR Botanical Adulterants Prevention Program.[1]

Scope

The continued demand for cranberry based supplements and beverages in the marketplace and the rising costs of cranberry raw material have seemingly served as an incentive for economically-motivated adulteration with synthetic colorants and/or anthocyanin- or proanthocyanidin (PAC)-rich extracts or PAC-rich materials (e.g., powders) from other, less expensive botanical sources. While admixture or substitution with synthetic colorants or anthocyanin-containing extracts can be detected rather readily, the inclusion of PACs from, for example, grape seed, peanut skin, or pine species in products purported to be cranberry extract is more difficult to detect and may require more advanced instrumentation, and/or a combination of analytical methods.

The evaluation of a specific analytical method or methods in this Laboratory Guidance Document for testing cranberry materials does not reduce or remove the responsibility of laboratory personnel to demonstrate adequate method performance in their own laboratory using accepted protocols outlined in various domestic (in the United States) or international legal and/or regulatory documents. Such documents include, for example, the 21 CFR Part 111 (Dietary Supplement GMPs, in the U.S. Code of Federal Regulations) and Part 117 (FSMA Final Rulemaking for Current Good Manufacturing Practice and Hazard Analysis and Risk-Based Preventive Controls for Human Food, in the U.S. Code of Federal Regulations), and by AOAC International, International Standards Organization (ISO), World Health Organization (WHO), and the International Council on Harmonisation (ICH).

3. Common and Scientific Names

3.1 Common name: cranberry

3.2 Other common names:

English: American cranberry, large cranberry, North American cranberry[2,3]
Chinese: *da guo yue jie* (大果越桔)[4]
French: canneberge, canneberge d'Amérique, canneberge à gros fruits, atoca, atoka, ronce d'Amérique[2,3]
German: Kranbeere, grosse Moosbeere[2–4]
Italian: ossicocco americano, mirtillo rosso canadese, mortelle di palude, cranberry[3]
Spanish: arándano, arándano americano, arándano trepador, arándano rojo[2–4]
Wampanoag: ibimi, sasumuneash[4]

3.3 Accepted Latin binomial name: *Vaccinium macrocarpon* Aiton

Note: Cranberry products on the dietary supplement, food and beverage markets are predominantly made from

Cranberry Products - Laboratory Guidance Document • 2018 • www.botanicaladulterants.org 1

There are important differences in the composition of various cranberry supplements on the market, particularly in regard to proanthocyanidin (PAC) concentrations. PACs are considered the main cranberry compounds responsible for preventing bacterial adhesion in the urinary tract. Concentrations vary from 0.8% to 24% in commercial cranberry extracts, with the majority of products containing between 0.8% and 1.5% PACs. Depending on the PAC concentration, bulk cranberry products were sold for $50 to $600 per kg in 2017.

The availability of lower-cost PACs from other plant sources, such as peanut (*Arachis hypogaea*, Fabaceae) skin or grape (*Vitis vinifera*, Vitaceae) seed, has led some unscrupulous suppliers to dilute or replace cranberry PACs — without labeling such dilution or replacement — for financial gain. Other known adulterants of cranberry include anthocyanin-rich extracts from other lower-cost sources. Anthocyanins range in color from red to blue, and anthocyanin-rich extracts are used to mimic the red color of authentic cranberry extracts. A summary of these methods of cranberry adulteration was published in BAPP's Cranberry Botanical Adulterants Prevention Bulletin in December 2017.

The new LGD was written by John H. Cardellina II, PhD, chief technical consultant for BAPP and a noted expert in natural products chemistry and analysis, and American Botanical Council (ABC) Chief Science Officer and BAPP Technical Director Stefan Gafner, PhD. The LGD evaluates the usefulness of published analytical methods to detect cranberry fruit product adulteration and summarizes the main advantages and disadvantages of each method. The document also details the chemical composition of cranberry fruit, potential confounding species, and known adulterants. The LGD was peer reviewed by 20 international experts from academia, the government, third-party contract analytical laboratories, and the herbal industry.

Gafner explained: "The variability in manufacturing processes and, accordingly, the composition of commercial cranberry ingredients make it challenging to find an analytical method that is able to detect all the different types of adulteration. Depending on the product specifications, a suite of test methods may be needed for unambiguous identification of a cranberry fruit extract."

Mark Blumenthal, ABC founder and executive director, and BAPP founder and director, said: "As with the case of other adulterated botanical materials on which we have reported, this new LGD provides a much-needed resource for industry and third-party analytical labs to ensure that they are using an analytical method that is robust and fit for purpose to detect the adulteration and fraud that is occurring in the global cranberry extract market."

Blumenthal added: "Older analytical methods may not be able to accurately detect the type of chemical manipulations that are used to adulterate cranberry materials in the marketplace, and any company that relies on some of the older, inadequate methods would be doing so at its own risk — that is, the company may be inadvertently 'approving' adulterated material."

Cardellina noted: "There has been a veritable explosion of interest and effort in developing suitable methods to ensure the authenticity and purity of cranberry products, whether they are juice- or extract-based. It is likely that further methodological studies will be reported in the near future, and BAPP will keep its stakeholders and the public apprised of such developments."

The cranberry LGD is the seventh publication in the series of LGDs published by BAPP. As with all of the program's publications, LGDs are freely accessible to all ABC members, registered users of the ABC website, and members of the public on the program's website (registration required). HG

—ABC Staff

Botanical Adulterants Prevention Program Publishes New Bulletin on Ashwagandha Root and Revised Bulletin on Saw Palmetto

The ABC-AHP-NCNPR Botanical Adulterants Prevention Program (BAPP) recently released a Botanical Adulterants Prevention Bulletin on ashwagandha (*Withania somnifera*, Solanaceae) root and root extract, and a revised bulletin on saw palmetto (*Serenoa repens*, Arecaceae) berry and berry extracts.

The goal of the Botanical Adulterants Prevention Bulletins is to provide accounts of ongoing issues related to botanical identity and adulteration. These bulletins allow quality control personnel and lab technicians in the herbal medicine, botanical ingredient, dietary supplement, cosmetic, herbal tea, conventional food, and other industries where botanical ingredients are used to stay informed about adulteration problems that are apparently widespread and/or imply safety concerns.

Ashwagandha Bulletin Describes Undeclared Addition of Leaf Materials to Root Products

The powdered roots of ashwagandha have a long history of use in Ayurvedic medicine, an ancient traditional medicine system in India, for a wide array of purposes: to treat inflammatory disorders, as an adaptogen for its immunomodulatory effects, to invigorate and strengthen the body, and to improve sexual stamina.

Ashwagandha is one of the most popular Ayurvedic herbs in the United States. It was the sixth top-selling dietary supplement in natural retail stores in 2017, with sales totaling roughly $10.6 million, a 25.6% increase from the previous year, according to the *HerbalGram* 2017 Herb Market Report.[1] Mainstream sales of ashwagandha supplements grew by more than 67% during the same period, but it did not make the list of the 40 top-selling supplements in this channel.


Botanical Adulterants Prevention Program

BOTANICAL ADULTERANTS PREVENTION BULLETIN

Adulteration of Ashwagandha (*Withania somnifera*) Roots, and Extracts

By Vineet Kumar Singh, MPharm,[a] Deepak Mundlinajeddu, PhD,[a] Amit Agarwal, PhD,[a] Jonathan Nguyen,[b] Sidney Sudberg,[b] Stefan Gafner, PhD,[c] Mark Blumenthal[c]

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Ashwagandha *Withania somnifera* Photo ©2019 Matthew Magruder

Various reports have described the addition of undeclared material from ashwagandha aerial parts (i.e., plant leaves and/or stems) to ingredients and products labeled to contain only ashwagandha root powders or root extracts. Aerial parts are typically available at a lower cost and contain some of the same types of chemicals (known as withanolides) as the roots.

The bulletin was a collaborative effort among Natural Remedies Private Limited (Bengaluru, India), Alkemist Labs (Garden Grove, California), and other members of BAPP. It summarizes the published data on ashwagandha adulteration, supply sources, market importance, and analytical methods to detect adulteration. Seventeen experts in quality control of medicinal plants from academia, government, and the herb industry provided input on the bulletin during the peer-review process.

"The inappropriate and unethical practice of increasing the amount of withanolides in ashwagandha root powder and extract by adding undisclosed, lower-cost dry leaf material and/or its extracts has been confirmed," said Mark Blumenthal, founder and executive director of the American Botanical Council (ABC) and founder and director of BAPP.

"This type of adulteration will fool only those companies and laboratories that do not use adequate analytical efforts to properly test their ashwagandha materials," he added. "A robust analytical methodology, such as high-performance thin-layer chromatography (HPTLC), or other methods that can provide the chemical fingerprint of withanolides, can determine if additional withanolides from undeclared leaf material are present.

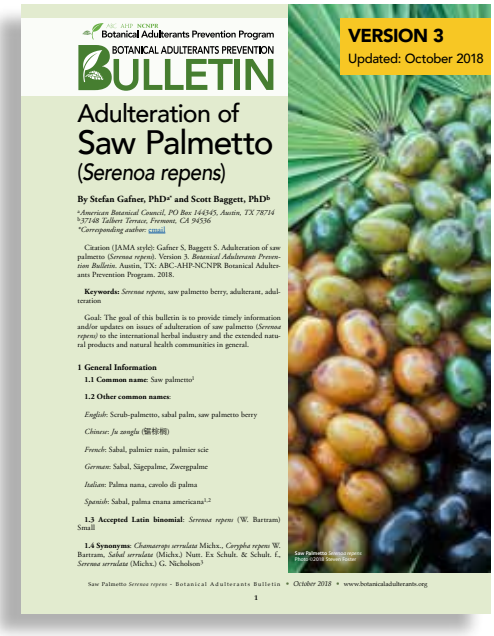
"We are aware of numerous companies that provide various types of authentic ashwagandha root raw materials and extracts," Blumenthal continued. "Our intention is to advise members of industry of the confirmed adulteration of some ashwagandha raw materials and extracts and for industry quality control laboratories to be doubly aware of the need for appropriate testing to authenticate the materials."

Stefan Gafner, PhD, chief science officer of ABC and technical director of BAPP, commented: "Herbal ingredients that have a history of use in Indian traditional medicine systems, and for which their benefits are supported by multiple clinical trials, have seen some of the highest sales increases in the United States in recent years. At the same time, these ingredients — which include boswellia (Indian frankincense; *Boswellia serrata*, Burseraceae), turmeric (*Curcuma longa*, Zingiberaceae), and ashwagandha, among others — reportedly have been subject to adulteration by unscrupulous suppliers. This supports the idea that there are clear links among market success, supply shortages, and adulteration."

Blumenthal added: "A key factor in adulteration is concealment. If a manufacturer chooses to openly combine ashwagandha root and leaf extracts into proprietary botanical products, this is appropriate so long as the labeling is transparent."

Updated Saw Palmetto Bulletin Highlights Fraudulent Blends Made with Animal-Based Fatty Acids

Saw palmetto fruit extract is a popular ingredient in dietary supplements in the United States and other countries and in phytomedicinal products in Europe. The primary use is for normalizing prostate function to relieve lower urinary tract symptoms related to benign prostatic hyperplasia (BPH) in middle-aged and older men. According to the 2017 *HerbalGram* Herb Market Report, saw palmetto products ranked among the 20 top-selling herbal supplements in the United States in both the natural and mainstream retail channels.[1]



As documented in the initial bulletin, which was published in February 2017, the addition of undeclared lower-cost oils (e.g., palm [*Elaeis guineensis*, Arecaceae], coconut [*Cocos nucifera*, Arecaceae], or sunflower [*Helianthus* spp., Asteraceae] oils) to saw palmetto extracts for financial gain has been known since the early 2000s. Over the past two years, several saw palmetto suppliers have reported the sale of a particularly sophisticated type of adulterated saw palmetto extracts mainly from manufacturers in Asian countries. According to the suppliers, these materials are made partly using fatty acids obtained from animal fats and are designed to mimic the fatty acid composition of authentic saw palmetto extracts. The revised saw palmetto bulletin has been updated to reflect this newly reported form of adulteration.

The bulletin was authored by Gafner and Scott Baggett, PhD, an analytical methods consultant for the natural products industry. Besides information on new forms of adulteration and how to detect them, the bulletin provides the latest saw palmetto sales data in the United States and a discussion of the new harvest permit requirements announced by the Florida Department of Agriculture and Consumer Services in July 2018. Six expert peer reviewers provided input on the revised saw palmetto bulletin. The first bulletin was peer reviewed by 10 experts.

Gafner explained: "Below-average harvests of saw palmetto berries have led to a dramatic increase in berry prices. This situation, combined with a consistently strong demand for saw palmetto dietary supplements and other phytomedicinal products, has led to a situation in which adulteration of saw palmetto extracts appears to be on the rise. Adulteration by mixing saw palmetto extracts with fatty acids from animal materials is particularly challenging to detect since these fraudulent mixtures are designed to pass routine laboratory chemical methods of analysis."

Blumenthal added: "Adding undisclosed amounts of animal fats to what would otherwise be a plant-based remedy is illegal and ethically inappropriate, particularly for the millions of people who are vegetarians or members of a religious group that promotes or requires vegetarianism or avoidance of certain types of meats."

About the ABC-AHP-NCNPR Botanical Adulterants Prevention Program

The ABC-AHP (American Herbal Pharmacopoeia)-NCNPR (National Center for Natural Products Research) Botanical Adulterants Prevention Program is an international consortium of nonprofit professional organizations, analytical laboratories, research centers, industry trade associations, industry members, and other parties with interest in herbs and medicinal plants. The program advises industry, researchers, health professionals, government agencies, the media, and the public about the various challenges related to adulterated botanical ingredients sold in commerce. More than 200 US and international parties have financially supported or endorsed the program.

As of January 2019, the program has published 48 extensively peer-reviewed documents, including *HerbalGram* articles, Botanical Adulterants Prevention Bulletins, Laboratory Guidance Documents, and Botanical Adulterants Monitor e-newsletters. All of the program's publications are freely available on the program's website. HG

—ABC Staff

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ADOPT-AN-HERB

HerbMedPro™ PROGRAM

The American Botanical Council's Adopt-an-Herb Program provides a mutually beneficial opportunity to support ABC's nonprofit educational efforts and promote a company's most important herbs.

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HerbMedPro provides online access to abstracts of scientific and clinical publications on more than 250 commonly used medicinal herbs. A free version, HerbMed®, is available to the general public and includes access to adopted herbs. HerbMedPro is available as a member benefit to all ABC members at the Academic Membership level and up.

In addition to ensuring that recently published information on an adopted herb is up to date on HerbMedPro, another benefit adopters enjoy is being included among their peers in each issue of ABC's acclaimed quarterly, peer-reviewed scientific journal, *HerbalGram*, on the ABC website, and at scientific, medical, and other educational conferences. Press releases also are issued on new adoptions, bringing attention to the program, the adopted herb, and the adopting company. Each adopted herb is featured on its own page on the ABC website.

Parties interested in taking part in the Adopt-an-Herb Program are invited to contact ABC Development Director Denise Meikel at 512-926-4900, extension 121, or by email at denise@herbalgram.org.

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Herbal Adopters

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Crocus sativus

Cayenne
Capsicum annuum

EpiCor® Fermentate
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Rhodiola rosea

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Baobab
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Rooibos
Aspalathus linearis

Propolis

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Plant name
Scientific name

NEW ADOPTER!

Senna
Senna alexandrina

Soladox BOTANICALS

Black Chokeberry
Aronia melanocarpa

Elderberry
Sambucus nigra

Stinging Nettle
Urtica dioica

Echinacea
Echinacea spp.

Purple Corn
Zea mays

Lemon Balm
Melissa officinalis

Bulbine
Bulbine natalensis

Broccoli
Brassica oleracea Broccoli Group

Tea Tree
Melaleuca alternifolia

Peppermint
Mentha x piperita

Aloe Vera
Aloe vera

Maca
Lepidium meyenii

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Plant name
Scientific name

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American Herbal Pharmacopoeia Publishes Monographs and Therapeutic Compendia for Belleric Myrobalan and Oshá

The American Herbal Pharmacopoeia (AHP) recently released two new monographs containing quality control standards and therapeutic compendia for belleric myrobalan (*Terminalia bellirica*, Combretaceae) fruit, which has a long history of medicinal use in its native India and Southeast Asia, and oshá (*Ligusticum porteri*, Apiaceae, and related species) root, a North American medicinal herb.

AHP monographs, which are available for purchase through AHP's website,[1] establish identification, purity, and quality standards for botanical raw materials and preparations. The therapeutic compendia provide a comprehensive review of pharmacological and safety data, including information on medical indications and supporting evidence from clinical, animal, and in vitro studies, modern and traditional uses, pharmacokinetics, pharmacodynamics, structure and function claims, dosages, interactions, side effects, contraindications, toxicology, and more. This information can be used by various individuals in the herbal community, from consumers and practitioners to quality control personnel, purchasing agents, and dietary supplement manufacturers.

Belleric Myrobalan: An Important Ayurvedic Herb

Notably, the fruit of *T. bellirica* is one of the three ingredients of the *triphala* ("three fruits") formula, along with the fruits of amla (*Phyllanthus emblica*, Phyllanthaceae) and chebulic myrobalan (*T. chebula*). Triphala is one of the most important and commonly used formulas in India's traditional medicine system of Ayurveda. AHP is also working on monographs and therapeutic compendia for the other two triphala fruit ingredients and the formula itself, which will be the first in a Western pharmacopeia.

The belleric myrobalan monograph, which was released in January 2019, was a collaboration among AHP; Pulok Kumar Mukherjee, PhD, of Jadavpur University in Kolkata, India; Bhushan Patwardhan, PhD, of Savitribai Phule Pune University in Pune, India; and Sarita Shrestha, MD, of the National Ayurveda Research and Training Center in Kathmandu, Nepal; among others. In all, 23 authors from around the world contributed to the monograph and therapeutic compendium, and 24 experts from academia, industry, and medical practice reviewed it before publication. Work on the monograph began in 2016.

Belleric myrobalan is a large deciduous tree that has pale greenish-yellow flowers and can grow to 30 meters (98 feet) tall. The small, gray, velvety fruits (drupes) are called *vibhitaka* in Sanskrit, which means "eliminating fear of disease" or "fearless." In Ayurvedic formulas, it is typically the deseeded fruit (pericarp) that is used, but the entire fruit is used regionally and traded commercially. Many ethnic groups throughout the species' range have used the fruit both internally and externally for many purposes, including for respiratory conditions such as cough, asthma, and bronchitis; eye conditions such as conjunctivitis; and skin conditions. However, the fruit is not typically consumed as food, largely because of its astringency.

According to Roy Upton, RH (AHG), DipAyu, president of AHP and editor of the monograph, the fruit has demonstrated anti-atherosclerotic, antifungal, antihyperuricemic, antimicrobial, anti-parasitic, antispasmodic, anti-ulcer, blood sugar-regulating, and hepatoprotective properties in preclinical research. "Many of these actions relate directly to promoting digestive and gastrointestinal health, which is one of the key applications of *T. bellirica* and triphala," he wrote (email, January 17, 2019).

Upton also added that because *T. bellirica* is an ingredient of what is probably the most important formula in Ayurveda, it is one of the most important herbs in the Indian materia medica. The monograph "is actually long overdue," Upton wrote. "Ayurveda is not well represented in this country, and it took a while to secure funding for the monograph."

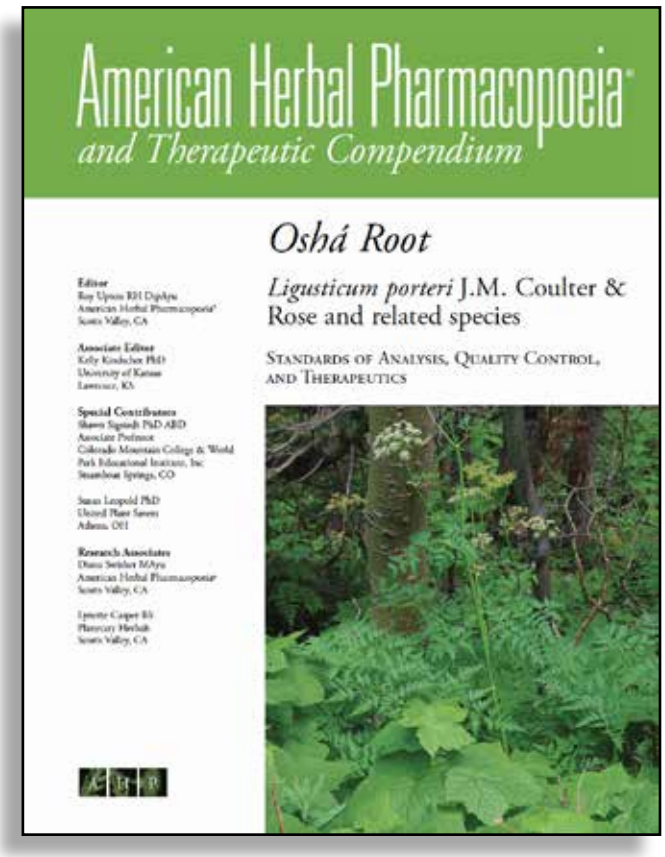
Commenting on the uniqueness of the species, Upton noted that the *Rigveda Samhita*, a collection of Sanskrit hymns and verses (ca. 1700-1100 BCE), includes the first known written record of *T. bellirica*. "Think of that: a botanical that has recorded history of use dating back almost 4,000 years," he wrote. "That in itself is very unique. Of the three fruits in triphala, this one has the most laxative properties but also has the toning qualities associated with the entire triphala formula.

"The combination of promoting peristalsis while simultaneously adding tonicity to tissues makes both triphala and *T. bellirica* unique," Upton continued. "This is in stark contrast to harsh laxatives that only stimulate peristalsis, making the bowels weaker over time. One of the most interesting things both about *T. bellirica* and triphala is that they are used for both constipation and diarrhea. They are highly effective lower bowel regulators."

In an AHP press release about the new monograph, Upton was quoted as saying: "I surveyed a number of Ayurvedic practitioners many years ago, and … triphala was regarded as their most important formula, with virtually every patient at some point in their treatment protocol receiving triphala. So, it is natural to develop monographs on the individual fruits. While the benefits of triphala are well known, this often causes the amazing benefits of its individual ingredients to be overlooked."

Mark Blumenthal, founder and executive director of the American Botanical Council, said: "With this newest publication, AHP adds another important herb to its growing list of botanicals for which it has produced high-quality, extensively peer-reviewed monographs, providing members of the herb community with reliable, authoritative quality control and therapeutic information. AHP is to be congratulated for its excellent works that help to promote the responsible trade in and uses of botanical ingredients and their products."

Publication of the belleric myrobalan monograph was made possible by the support of Amsar Goa Pvt. Ltd., Aveda Corporation, Banyan Botanicals, East West School of Planetary Herbology, Gaia Herbs, NuAxon Bioscience Inc., Organic India Charitable Trust, Phalada Agro, Planetary Herbals, Pukka Herbs, The Ayurvedic Institute, Verdure Sciences, and Vikram Nahawar.



Oshá: A Native American Botanical

According to AHP, the oshá monograph, which was released in December 2018, includes the first published pharmacopeial standards for this North American botanical.

The publication is the result of a collaboration among AHP; Kelly Kindscher, PhD, of the University of Kansas; and the United Plant Savers (UpS), and was partially funded by the American Herbal Products Association Foundation for Education and Research on Botanicals (AHPA-ERB Foundation). Special contributions were made by Shawn Sigstedt, PhD, of Colorado Mountain College and Healing Planet Herbs, Inc., who has dedicated much of his life to the study of oshá. Fourteen authors contributed to the monograph and therapeutic compendium, and 28 experts from academia, industry, and medical practice reviewed it before publication. The work for the monograph began in 2014, after Kindscher, the publication's associate editor, received a grant from the AHPA-ERB Foundation to conduct a sustainability assessment on the impact of wild collection on oshá populations.

The monograph opens with an extensive history section that details oshá's traditional uses by Native American tribes, its introduction to modern-day herbal practice, and how animals, specifically bears, have used it to self-medicate (i.e., zoopharmacognosy). Another common name for oshá is "bear root." Ethnobotanists have recorded bears both in captivity and in the wild chewing oshá roots and rubbing against the plant. Also, in one remarkable account, a bear applied the root to its own gunshot wounds.

Multiple species in the Apiaceae family are referred to as "oshá," including *L. canbyi*, *L. filicinum*, *L. grayi*, *L. tenuifolium*, and *Conioselinum scopulorum*. According to Upton, who edited the monograph and therapeutic compendium, the recognition of other species as oshá is important because, while AHPA's *Herbs of Commerce*, 2nd edition, lists only *L. porteri* as an accepted species,[2] these closely-related species are difficult to distinguish in the wild, and many are used interchangeably. Because oshá cultivation is limited and much of the available product in commerce is wild-harvested, knowledge of these species and their subtle morphological

differences is especially important for quality control initiatives and sustainability.

Oshá is a high-altitude plant with extensive ritualistic and medicinal traditions of use by Native American tribes in its native range: northern Mexico and the southwestern United States, Pacific Northwest, and Rocky Mountains. Modern herbalists primarily use oshá root for respiratory infections and other upper respiratory disturbances, including cough. In vitro studies have confirmed the antimicrobial effects of oshá root essential oil. The hormone melatonin and neurotransmitter serotonin also have been identified in *L. porteri* and *L. canbyi*, which suggests that oshá root may have potential positive effects on mental health.

According to Upton: "I first learned of oshá from a Navajo friend, Molly Olivas, whose uncles used it to keep away rattlesnakes. They would tie it to their boots when hunting. I was then introduced to lovage [*Levisticum officinale*, Apiaceae] by California herbalist Bea Meyers, who asked me to pick it from her garden. I was amazed at how similar they were. I swore the lovage was oshá. That was the genesis of broadening our reach beyond a single species.

"I am sincerely grateful for the financial support provided by UpS and the AHPA-ERB Foundation, and that they saw the development of the monograph as a natural extension of conducting formal population studies," Upton continued. "Oshá is such an important traditionally used herb that we have to have a knowledge base, both to know how to use it and to know how to protect it. Sometimes understanding or emphasizing when not to use something is more important than knowing its benefits. The *Ligusticum* genus is populated with amazing botanicals, many with similar activity, so we have to think broadly when considering the use of oshá."

Blumenthal said: "I am quite familiar with various medicinal uses of this wild aromatic root from my days in the mountains of northern New Mexico, where oshá grows near mountain stream beds. It is prized as a local traditional medicinal plant by Native Americans and the local Hispanic population, but it never has achieved much popularity in the US herb industry, being sold mainly by small regional and national herb extract companies. This is probably preferable, since there is a supply sustainability issue with oshá, and it is difficult to cultivate this plant in a commercially viable manner."

The oshá monograph was made possible by the support of the AHPA-ERB Foundation, Herbs Etc., Vitality Works, UpS, Mountain Rose Herbs, Maryland University of Integrative Health, and Sheila and Tim Manzagol. HG

—Connor Yearsley and Hannah Bauman

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Chamomile and Damask Rose Aromatherapies Reduce Pain and Anxiety during Childbirth

Anxiety and pain can have a significant impact on childbirth and may predispose pregnant women to certain complications. Fear of pain is the most common reason for elective cesarean delivery, and anxiety and stress may reduce uterine contractions, increasing the duration of labor and possibly the likelihood of instrumental or cesarean delivery. Anxiety also increases the perception of pain severity and decreases pain tolerance during labor.

Aromatherapy with herbal essential oils (EOs) may help reduce anxiety and pain, and thus labor duration. Several EOs have been studied for their effects during labor, and many women have reported positive effects on pain and anxiety with EO therapy. The authors of two recent clinical trials evaluated the effects of chamomile (*Matricaria chamomilla* syn. *M. recutita*, Asteraceae) and Damask rose (*Rosa* × *damascena*, Rosaceae) aromatherapy on contraction intensity, pain, and anxiety in women during labor.

Chamomile Aroma Reduces Contraction Intensity in First Birth Experience

Reviewed: Heidari-Fard S, Mohammadi M, Fallah S. The effect of chamomile odor on contractions of the first stage of delivery in primpara [sic] women: A clinical trial. *Complement Ther Clin Pract*. August 2018;32:61-64. doi: 10.1016/j.ctcp.2018.04.009.

Chamomile has long been a popular medicinal plant used for a wide range of health conditions. EOs from the flowers are used as a calming agent in aromatherapy and may provide benefits in reducing pain and stress during labor. In this two-armed, randomized, controlled trial, researchers explored the effects of chamomile aromatherapy on the birthing experience of women delivering their first child. The study focuses on labor contractions and overall satisfaction with the birthing experience.

For the study, 130 pregnant women (18-35 years of age) were recruited at the Emdadi Hospital in Abhar, Iran. Included participants were between 37 and 42 weeks of gestation and carrying a single, healthy fetus of normal weight. They also had a normal pelvis and body mass index; had no history of sensory abnormalities, acute or chronic psychological disease, pain, or allergy to chamomile; did not use narcotics eight hours before the active stage of delivery; and had three to five contractions per minute. Participants were excluded from the analysis if they had an induced delivery or experienced any problems during delivery, such as abnormal fetal heart rate, prolapsed placenta, or lack of labor progress.

Data were collected before, during, and after labor using a form designed by the researchers. A panel of 10 faculty members of the Shahid Beheshti School of Nursing and Midwifery reviewed the form, and the researchers revised it based on their suggestions. Collected data included demographic and maternal information, examination and observation information (including findings from vaginal exam, Bishop score, cervical dilation, and vital signs throughout), and birthing satisfaction using a Likert scale of "satisfied," "relatively satisfied," and "dissatisfied."

Study Details: At a Glance	
Study Design	Randomized clinical trial
Participants	130 primiparous women
Study Length	Duration of first stage of labor
Test Material	Chamomile aromatherapy
Control	Water
Disclosures	None reported

Chamomile *Matricaria chamomilla*
Photo ©2019 Steven Foster

The experimental chamomile EO was produced by the Zardband Pharmaceuticals Company in Tehran, Iran. Water was used as the control. The intervention began at dilation of 4 cm and continued until the end of delivery. Two drops of EO or control were applied to a gauze pad, which was held 7-10 cm from the nose of the laboring participant (for an unstated amount of time) every 30 minutes for a total of three times during each dilation range. The participants were asked to smell the gauze pad. Blinding was not possible due to the distinctive scent of chamomile.

Researchers analyzed the number, duration, and intensity of contractions at dilations of 3-4, 5-7, and 8-10 cm, as well as subjective satisfaction scores. There were no statistically significant differences between the two groups in demographic data. The mean age of participants was 25 years, approximately 90% of the pregnancies were described as "unwanted," approximately 10% of participants had received a higher education diploma, and approximately 72% were employed. An independent t-test, χ^2 test, and Mann-Whitney U test were used to analyze the data.

No statistically significant differences were found between the two groups in duration of contractions (determined using a "standard Citizen watch") or number of contractions. As for intensity of contractions (assessed by a "manual check of the abdomen"), no significant differences between groups were found at 3-4 or at 8-10 cm of dilation. However, in the chamomile group, contractions at 5-7 cm dilation were significantly less intense than in the control group ($P = 0.004$). During this phase, 16.9% of participants in the control group had moderate contractions, and 83.1% had strong contractions. In the chamomile group, 29.2% of participants had moderate contractions, and 70.8% had strong contractions. One person in the intervention group and two people in the control group were excluded due to emergency caesarean sections.

Participants receiving chamomile aromatherapy were significantly more satisfied with their birthing experience than those in the control group (64.6% vs. 0%; $P < 0.0001$). In addition, significantly more subjects in the chamomile aromatherapy group said they would use the method again in future deliveries (81.5% vs. 21.5%; $P < 0.0001$).

Satisfaction with the birthing process can have long-lasting benefits for mothers, their children, and family relationships. Other studies have shown that aromatherapy during labor using lavender (*Lavandula angustifolia,* Lamiaceae) EO and an EO blend containing chamomile increases satisfaction and reduces pain during labor. According to the authors, this is the first study to evaluate the effects of aromatherapy during labor using chamomile EO only. The findings of this study are preliminary and more research is needed, especially to compare chamomile to other EOs. Furthermore, ruling out a placebo effect is needed, but this is challenging with aromatherapy treatments. Nonetheless, the authors suggest that chamomile EO aromatherapy is a safe, cost-effective method to improve the birthing experience.

Study Details: At a Glance	
Study Design	Randomized, controlled clinical trial
Participants	110 nulliparous women
Study Length	Duration of first stage of labor
Test Material	*Rosa damascena* essence aromatherapy
Control	Saline solution aromatherapy
Disclosures	None reported

Damask Rose Aromatherapy Reduces Pain and Anxiety

Reviewed: Hamdamian S, Nazarpour S, Simbar M, Hajian S, Mojab F, Talebi A. Effects of aromatherapy with *Rosa damascena* on nulliparous women's pain and anxiety of labor during first stage of labor. *J Integr Med*. March 2018;16(2):120-125. doi: 10.1016/j.joim.2018.02.005.

Damask rose is used in traditional herbal medicine for its relaxant, antitussive, hypnotic, antioxidant, antibacterial, and antidiabetic effects, which are mostly attributed to its phenolic compounds. Damask rose essential oil (DREO), extracted from flower petals

via steam distillation, has been shown to have antispasmodic, analgesic, anti-inflammatory, and antidepressant properties. Potentially active compounds include linalool, nerol, geraniol, 1-nonadecene, n-tricosane, hexatriacontane, and n-pentacosane. Massage with DREO, in addition to aromatherapy, may be beneficial in dysmenorrhea and for reducing menstrual bleeding. DREO also is used to treat premenstrual symptoms and postpartum depression.

The authors conducted the first study of the effects of DREO aromatherapy on pain and anxiety of first-stage labor in a single-blinded clinical trial. Sample size was calculated to be 116 (58 per study arm), assuming a two-sided 5% significance level, power of 80%, and loss of 10% of subjects due to severe pain or obstetric complications. Parturient women (i.e., women about to give birth) experiencing a singleton, full-term, non-complicated, cephalic-presentation pregnancy, with adequate prenatal care and no history of allergy, were recruited at a hospital in Jajarm, Iran.* Exclusion criteria included severe pain, unexpected emergency, or symptoms of potential allergy during the intervention. Participants were randomly assigned to the intervention group or control group, but it appears that randomization had to be done by day, rather than by individual, because only one study substance (DREO or saline control) was provided to the clinic each day. This precaution was taken to preserve single blinding, due to DREO's aroma. Researchers distilled one batch of DREO for the study, diluted to 2% with sesame (*Sesamum indicum*, Pedaliaceae) seed oil. Participants were told they would be given an inhaled liquid for pain, but not whether it would have an odor.

Data were collected via a demographic and fertility questionnaire completed by women upon consenting to join the study, an observational examination checklist completed by caregivers, a numerical pain rating scale, and the Spielberger anxiety questionnaire. Standard aromatherapy procedures, involving the attachment of a gauze pad moistened with DREO or saline to the collar, were initiated when cervical dilation reached 4 cm and continued until delivery. Severity of pain was measured 10 minutes after inhalation of DREO or saline aroma at three points of cervical dilation (4-5, 6-7, and 8-10 cm), between uterine contractions. Anxiety was assessed 10 minutes after inhalation at two points of cervical dilation (4-7 cm and 8-10 cm). All routine care practices were performed for all participants. Apgar scores (an assessment of infant health) from the first and fifth minutes after delivery and infant weights also were recorded.

The two study groups were not significantly different in their demographic and fertility characteristics or in their characteristics of labor, including duration and number of contractions, use of oxytocin to induce labor, and Bishop scores. Of 116 participants, 110 completed the study (55 in each arm). Six were excluded due to severe pain, emergency cesarean section, or bleeding. Pain severity in the DREO group was significantly lower than in the saline group at every data collection point ($P < 0.05$ for all). Anxiety levels were also significantly lower with DREO than control ($P < 0.05$ at both points). There were no significant between-group differences regarding mode of delivery or infant Apgar scores.

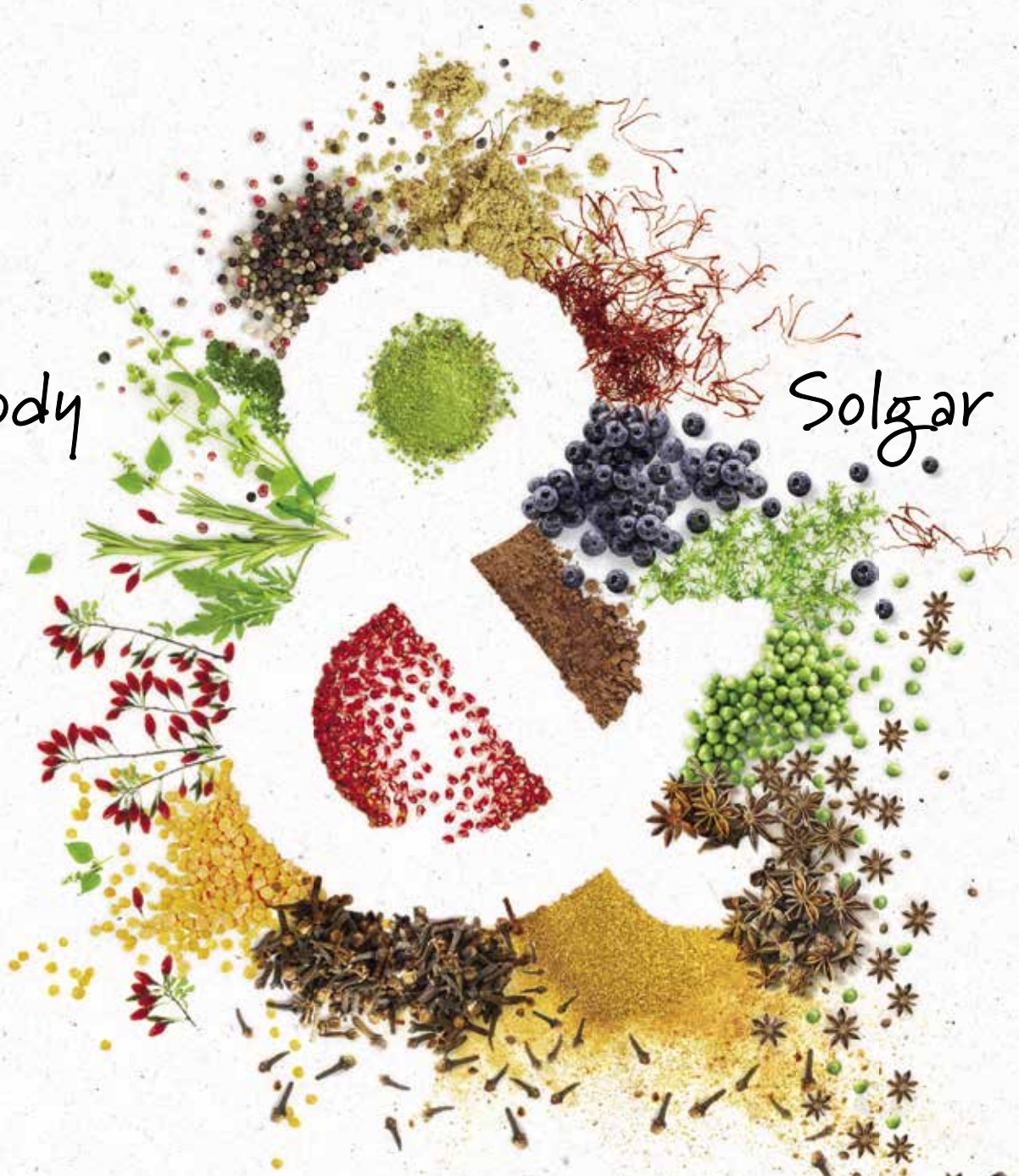
Results indicate that DREO may be a safe, useful, and inexpensive treatment for pain and anxiety during labor. The authors note that individual pain tolerance is variable and could not be controlled for since only subjective pain measures were used. HG

—Anne Louise Merrill and Mariann Garner-Wizard

Damask rose *Rosa damascena*
Photo courtesy of Pxhere.com

* Although the report includes "nulliparous" in its title, and one mention is made of patients being primiparous, previous pregnancy is not explicitly listed as an exclusion criterion.

Body Solgar



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Systematic Review of Herbal Medicines for Depression and Anxiety in Menopausal Women

Reviewed: Fattah A. Effect of phytoestrogen on depression and anxiety in menopausal women: A systematic review. *J Menopausal Med*. December 2017;23(3):160-165. doi: 10.6118/jmm.2017.23.3.

Symptoms of menopause may include mood disturbances such as mood swings, irritability, anxiety, and depression.* Conventional treatments for menopausal symptoms include hormone therapy (HT), which is associated with an increased risk of cardiovascular events and breast cancer, and antidepressant medications such as selective serotonin reuptake inhibitors (SSRIs), which can cause adverse effects such as sleep disturbances, weight gain, diarrhea, and sexual dysfunction.

The author of this review conducted a systematic search of MEDLINE (1966-March 2017), Scopus (1990-March 2017), and the Cochrane Library (Cochrane Central Register of Controlled Trials; 2017) using various keywords related to anxiety, depression, and commonly used herbal treatments for symptoms of menopause. There were no language restrictions, and references were hand-searched. Included studies were randomized, controlled, parallel or crossover trials that included perimenopausal or postmenopausal women with depression or anxiety. The Consolidated Standards of Reporting Trials (CONSORT) checklist was used to evaluate study quality.

A total of 1,786 studies were identified, and nine met the inclusion criteria. The studies evaluated four herbs, includ-

Study Details: At a Glance	
Study Design	Systematic review
Included Studies	Nine randomized, controlled clinical trials
Study Length	12-24 weeks
Test Materials	Preparations of various botanicals, including soy, hops, kava, and red clover
Controls	Various
Disclosures	None reported

* Some scientists contest that depression is a symptom of menopause. It may be coincidental to menopause and more due to cultural values favoring youth as women are getting older, secondary to sleep problems due to menopause, and other factors — but not menopause itself.

Soy *Glycine max*
Photo ©2019 Steven Foster

Hops *Humulus lupulus*
Photo ©2019 Steven Foster

ing soy (*Glycine max*, Fabaceae), hops (*Humulus lupulus,* Cannabaceae), kava (*Piper methysticum*, Piperaceae), and red clover (*Trifolium pratense*, Fabaceae).

Three studies evaluated the effects of soy on symptoms of depression and/or anxiety. The first was a small study that compared the effects of soy flour (100 mg isoflavones) (n = 7) with a placebo of wheat (*Triticum* spp., Poaceae) grain cereal (n = 12) for 24 weeks. Neither group experienced a significant improvement in depression compared with baseline. The second study compared 12-week treatment with soy protein (n = 44; dose not reported) to placebo (n = 50). The soy group experienced a 25% improvement in depression scores from baseline, compared with no change in the placebo group (*P* value not reported). There was no difference between groups in the anxiety score post-treatment. The third study evaluated soymilk (n = 15; dose not reported), soymilk plus exercise (n = 12), or placebo (n = 10) for 12 weeks; there was no significant difference in depression or anxiety among groups. "To sum up, soy slightly improved anxiety and depression," wrote the author of the review. However, this conclusion may not be warranted considering the small sample size of two of the included trials, the differences in soy products, and that only one of the three trials found an improvement in depression only.

One study evaluated the effects of hops on depression and anxiety using the Greene Climacteric Scale, a questionnaire that assesses various mental, physical, and vasomotor symptoms of menopause. Patients received placebo (n = 60) or 500 mg/day of powdered hops corymbs (flower clusters) (n = 60) for 12 weeks. Hops significantly decreased anxiety and depression compared with placebo at two, four, eight, and 12 weeks ($P < 0.001$ for all).

One study evaluated the effect of kava on depression and anxiety. For 12 weeks, patients took 100 mg/day kava rhizome extract (containing 55% kavain; Natural Bradel; Milan, Italy) plus 1 g/day calcium (n = 15), 200 mg/day kava plus 1 g/day calcium (n = 19), or 1 g/day calcium only (n = 34). There was a significant decrease in depression at three months in the 200 mg/day kava group compared with baseline (*P* value not reported) but not compared to the calcium-only group. Compared with baseline, there was a significant decrease in anxiety at three months in the 100 mg/day and 200 mg/day kava groups but not the calcium-only group (*P* values not reported). This study did not report a placebo group.

Four studies evaluated the effects of red clover on depression and anxiety. One of these treated patients with red clover extract (n = 50; dose not reported; described in the original paper as "MF11RCE," containing 80 mg red clover isoflavones) or placebo (n = 59) for 12 weeks. On the Zung Self-Rating Depression Scale, the red clover group experienced a significant improvement compared with both baseline and placebo ($P < 0.001$ for both). In a separate 12-week study, patients were assigned to one of three groups: placebo (n = 85), Promensil (PharmaCare Laboratories; Warriewood, NSW, Australia; n = 85), or Rimostil

Red clover *Trifolium pratense*
Photo ©2019 Steven Foster

Kava *Piper methysticum*
Photo ©2019 Steven Foster

(Novogen Ltd.; Plédran, France; n = 83). Promensil and Rimostil are dietary supplements that each provide 82 mg of red clover isoflavones. Anxiety and depression scores did not differ significantly among the groups after 12 weeks. Another study evaluated 80 mg red clover or placebo for 12 weeks in a crossover study (n = 53) with a one-week washout period. The red clover groups exhibited a significant improvement in depression and nervousness (P = 0.05 for both). In the fourth study, participants who received an ethanolic extract of red clover aerial parts (standardized to 120 mg/day isoflavones) (n = 22**) for 12 months experienced significantly reduced Greene anxiety scores at the end of the study, compared to placebo (n = 17) (P = 0.04) in a double-blind trial. The anxiety score was a secondary outcome; primary outcome measures were the reduction of occurrence and intensity of hot flashes and night sweats.

The quality ratings for the individual trials are not clearly indicated. The author of the review reported that "the random sequence generation, allocation concealment and blinding of outcome assessment was either not performed or not reported in sufficient detail in most of [the] studies. The overall methodological quality was moderate to high."

The author concluded that soy may have a beneficial effect on anxiety and depression, red clover findings are inconclusive, and 200 mg/day of kava and 500 mg/day of hops may be beneficial for anxiety and depression. However, the author cautioned that, in general, "beneficial effects still remain indeterminate due to poor methodology, limited RCTs and small sample size."

Limitations of this review article include: incomplete literature searches (several eligible trials were not included), inaccurate or incomplete reporting of results, unfounded conclusions regarding soy and kava, unreported doses and/or manufacturers of some herbal products, grammatical and typographical errors, and a misleading title (some of the included botanicals do not contain phytoestrogens). Also, the standardization of the products was not described. Therefore, it is difficult to make any conclusions from the reported studies becuase the analyzed botanical products could vary widely in chemical composition and thus in biological activity. HG

—Heather S. Oliff, PhD

** The review article incorrectly reported the number as 14; the original study publication reports n = 22.

Cinnamon Improves Various Metabolic Risk Factors in Women with Polycystic Ovary Syndrome

Polycystic ovary syndrome (PCOS) is associated with irregular menstrual cycles, chronic anovulation, and hyperandrogenism, as well as metabolic aberrations such as insulin resistance (IR), hyperinsulinemia, and dyslipidemia. PCOS is diagnosed when a woman has two of the following conditions with no other medical explanation: hyperandrogenism, intermittent or absent menstrual cycles, and polycystic ovary indicated by ultrasound. Although its etiology is uncertain, PCOS appears to result from a combination of genetic and environmental factors.

IR is common in women with PCOS, may play a causal role in its development, and can contribute to the development of obesity, type 2 diabetes, and cardiovascular problems. Pharmaceutical treatments for PCOS are limited by contraindications, poor efficacy, and adverse effects. Cinnamon (*Cinnamomum verum*, Lauraceae) bark is used in traditional Persian medicine to regulate menstrual cycles in patients with PCOS, and it has been shown to lower blood glucose and reduce the homeostatic model assessment of insulin resistance (HOMA-IR) index, a measure of insulin sensitivity, in patients with diabetes.

Two recent double-blind, randomized, controlled clinical trials evaluated the effects of cinnamon supplementation on metabolic factors such as serum insulin, HOMA-IR index, lipid profiles, and levels of adiponectin (a protein hormone that regulates the metabolism of lipids and glucose) in women with PCOS.

Cinnamon Bark Supplementation Results in Improvements in Insulin and Lipid Profiles

Reviewed: Borzoei A, Rafraf M, Asghari-Jafarabadi M. Cinnamon improves metabolic factors without detectable effects on adiponectin in women with polycystic ovary syndrome. *Asia Pac J Clin Nutr*. 2018;27(3):556-563. doi: 10.6133/apjcn.062017.02.

From October 2015 to February 2016, investigators recruited 84 women with PCOS who visited the gynecology clinic at Moheb Yas Hospital in Tehran, Iran. Included patients were 20 to 38 years old and had a body mass index (BMI) of 25-40 kg/m^2. The patients were categorized according to age and BMI and then randomly assigned to one of two groups of 42 participants each. At baseline, the patients' height and weight were measured, and a three-day average for energy and macronutrient intake was determined (using a patient recall method) for each patient. The groups were similar in anthropometric, dietary, and biochemical characteristics at baseline.

Cinnamon bark was provided by the Iranian Institute of Medicinal Plants in Tehran and was ground and encapsulated by the investigators. Each capsule contained 500 mg cinnamon (*Cinnamomum verum* syn. *C. zeylanicum*, Lauraceae) bark powder. Placebo capsules were filled with wheat (*Triticum aestivum*, Poaceae) flour. Each group took three capsules daily for eight weeks.

Study Details: At a Glance	
Study Design	Randomized, double-blind, placebo-controlled trial
Participants	84 overweight or obese women with PCOS (20-38 years of age)
Study Length	Eight weeks
Test Material	Capsules containing *Cinnamomum verum* bark powder
Control	Placebo capsules containing wheat flour
Disclosures	Financial support provided by the Research Vice-Chancellor of Tabriz University of Medical Sciences in Tabriz, Iran.

Cinnamon sticks *Cinnamomum* spp.
Photo ©2019 Steven Foster

Fasting blood samples were collected at baseline and after eight weeks to determine serum insulin, HOMA-IR, total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C) levels.

All patients completed the study, with a 94% compliance rate. No adverse effects were reported.

In the cinnamon group, significant decreases were seen in weight ($P < 0.01$) and BMI ($P = 0.002$) after eight weeks compared to baseline, while no significant changes were seen in the control group. In the cinnamon group, intakes of energy ($P = 0.02$) and total fat ($P = 0.04$) decreased and intake of protein increased ($P = 0.04$) after eight weeks, compared with baseline values.

Significant improvements were seen in serum glucose (10.63% decrease; $P < 0.01$), insulin (12.63% decrease; $P = 0.01$), and HOMA-IR index (20.25% decrease; $P < 0.01$) in the cinnamon group after eight weeks, compared with baseline values. Changes in the control group were not significant. Significant improvements from baseline in all lipid variables were seen in the cinnamon group after eight weeks ($P < 0.05$ for all). No significant changes were seen in the control group.

With adjustments for energy intake, BMI, and other baseline values, significant between-group differences were observed in serum glucose ($P = 0.001$), insulin ($P = 0.007$), HOMA-IR index ($P = 0.001$), TC ($P = 0.04$), LDL-C ($P = 0.04$), and HDL-C ($P = 0.001$) over the length of the study, with greater improvements seen in the cinnamon group. Between-group differences in serum TG levels were not significant. Changes in serum adiponectin levels, which were within normal limits at baseline, were not significant between the groups after eight weeks. "It seems that detected favorable effects on serum glucose and lipid parameters in our study were not mediated via adiponectin," wrote the authors.

Limitations of this study include its short duration, the use of a fixed dose of cinnamon, and the inclusion of patients whose BMI was 25 kg/m^2 or greater. The results may not be applicable to underweight or normal weight patients with PCOS or to consumption of other doses or durations of cinnamon supplementation.

The authors concluded that "short term supplementation of cinnamon had some favorable effects on metabolic risk factors of women with PCOS and may be useful in management of PCOS complications."

Cinnamon Powder Improves Insulin Resistance

Reviewed: Hajimonfarednejad M, Nimrouzi M, Heydari M, Zarshenas MM, Raee MJ, Jahromi BN. Insulin resistance improvement by cinnamon powder in polycystic ovary syndrome: A randomized double-blind placebo controlled clinical trial. *Phytother Res*. February 2018;32(2):276-283. doi: 10.1002/ptr.5970.

Conducted at Shiraz University of Medical Sciences in Shiraz, Iran, this study assessed the effects of cinnamon bark powder on insulin resistance in women with

Cinnamon *Cinnamomum verum*
Photo ©2019 Steven Foster

Study Details: At a Glance	
Study Design	Randomized, double-blind, placebo-controlled trial
Participants	66 women with PCOS
Study Length	12 weeks
Test Material	Capsules containing 500 mg cinnamon bark powder
Control	Placebo capsules containing 450 mg starch and 50 mg cinnamon bark powder
Disclosures	None reported

PCOS. Fresh cinnamon bark, purchased from a local market, was washed, dried, and ground into a powder, which was used to fill 500-mg capsules. Unfortunately, the authors did not mention the species of cinnamon* used in the study; they note only that the cinnamon sample "was identified by a botanist at the Shiraz School of Pharmacy with a specified voucher sample (no. 996)." Placebo capsules contained 450 mg of starch (heated until it turned brown) and 50 mg of cinnamon powder (used to produce similar taste and odor).

Patients at the University's Shahid Motahari Outpatient Clinic who were aged 18 to 45 years, met the Rotterdam Criteria for PCOS, and had a BMI of 18 kg/m^2 or greater were eligible for the study. Exclusion criteria included diabetes, hypertension, hyperprolactinemia, or thyroid problems, pregnancy or lactation, treatment for infertility, or use of hormones or any drug that affects insulin sensitivity. Enrollment took place between January 2016 and July 2016. Of 80 women screened, 66 were enrolled in the trial. For 12 weeks, 33 of those patients were instructed to take one cinnamon capsule three times daily after meals, for a total daily dose of 1,500 mg. The remaining 33 patients were instructed to take one placebo capsule three times daily. All patients also took a standard treatment of 10 mg daily of medroxyprogesterone for 10 days per month starting on day 15 of each menstrual cycle.

The primary outcome of the study was insulin resistance, as measured by the HOMA-IR index. Secondary outcomes were patients' anthropometric profiles (weight, BMI, and waist circumference); biochemical parameters including fasting blood sugar (FBS), two-hour postprandial blood glucose, and lipid profile; and androgenic hormone assays to measure total serum testosterone and dehydroepiandrosterone sulfate levels.

Three patients in the cinnamon group and two in the placebo group were not included in the final analyses because they missed follow-up visits. One patient in the cinnamon group discontinued the treatment because of a rash and itching, and one patient in the placebo group withdrew from the study because of travel plans. Four others, one in the cinnamon group and three in the placebo group, were noncompliant (they missed more than three doses) but were included in the intention-to-treat analyses. The final analyses included 29 patients in the cinnamon group and 30 patients in the placebo group.

Compared with the placebo group, the cinnamon group had significantly greater reductions in fasting insulin (P = 0.024), HOMA-IR index (P = 0.014), and LDL-C levels (P = 0.049) after 12 weeks. Fasting insulin and HOMA-IR declined substantially over the course of the study in both groups, though significantly more so in the cinnamon group.

Improvements from baseline were observed in the cinnamon group in body weight, BMI, waist circumference, FBS, two-hour postprandial blood glucose, TC, TG levels, and serum androgenic hormone levels. However, the changes were mostly small, and final figures were not significantly different from those in the placebo group. Testosterone levels significantly decreased in the cinnamon group from 0.82 ± 0.82 ng/mL at baseline to 0.55 ± 0.28 ng/mL at the end of the study (P = 0.001); there was also a smaller significant decrease (P = 0.041) in the placebo group.

The rash and itching reported by one patient in the cinnamon group disappeared after the treatment was discontinued. No other serious adverse effects were reported.

The use of progesterone therapy as standard treatment along with the study intervention in both groups is a limitation of this study, as the authors could not evaluate the effects of cinnamon on the patients' menstrual cycles. The therapy was used, however, because it was considered unethical to deprive any patient of standard medical treatment. Although the first evaluation of androgen was conducted during the follicular phase of all patients, final blood samples were drawn at the end of the study at 12 weeks, when some patients may have been in different phases of their menstrual cycle. According to the authors, this should be considered when interpreting the results of the androgenic hormone assays.

Other limitations of this study include the lack of an ultrasound of the patients' ovaries at the end of the study, the small number of patients, the short duration, and the failure to report the species of cinnamon used. The fact that the placebo contained a small dose of cinnamon may have reduced differences between groups, although the differential in dosage was 10-fold. Nevertheless, previous clinical research has suggested a relatively wide variability in daily dosage of cinnamon having an impact on serum glucose levels and other hemodynamic factors.

The authors concluded that "cinnamon supplementation with the daily dose of 1.5 g for 12 weeks in combination with progesterone therapy was well tolerated and significantly improved insulin sensitivity and decreased insulin and LDL level[s] in women with PCOS." HG

—Shari Henson

* A peer reviewer of this article noted that the species appears to be *C. aromaticum* based on the essential oil data included in the paper, but this has not been confirmed. The study authors did not respond to a request for more information.

GUEST EDITORIAL

Left: **Thyme** *Thymus vulgaris*
Center: **Eleuthero** *Eleutherococcus senticosus*
Right: **Lavender** *Lavandula angustifolia*
Photos ©2019 Steven Foster

ANCIENT MEDICINE FOR MODERN WOMEN

A Q&A with Herbal Physicians

By Tieraona Low Dog, MD, and Aviva Romm, MD

Women's history is woven together with plants and the healing arts, particularly botanical medicine and midwifery. In virtually every culture, women maintained knowledge of herbal healing for the prevention and treatment of common maladies that afflicted their communities, including, notably, treatments for women's concerns.

Because transmission of herbal knowledge historically was suppressed and marginalized, information on the practices of women healers must be "carefully teased out of a few surviving works written by women healers, from relics and artifacts, from myth and song, and from what was written about women."[1] And because of their exclusion from medical institutions, even well into the early 20th century, women had to use products from the natural world around them to treat their communities, especially women and children. Women's medicine has always been largely based on herbal therapies, yet rarely were the contributions of these female herbalists recognized by conventional medical history. For example, the "discovery" of foxglove (*Digitalis* spp., Plantaginaceae) as a treatment for cardiac conditions is attributed to Sir William Withering, and the treatment's alleged source, a woman herbalist who maintained a recipe book in which she apparently described employing the herb in a formula for dropsy (edema in the lower legs), is largely forgotten.

Although women have long handed down herbal knowledge to their daughters, both orally and in the form of "stillroom" books — the herbal equivalent of family recipe books — only a minority of women from the most privileged, educated backgrounds managed to keep comprehensive records or documentation of herbal "recipes." While a rare few contributed tomes to the herbal canon on women's, and general, health (Hildegarde of Bingen and *The Trotula* [a 12th-century collection of Italian texts on medicine for women's health], for example), these, too, were largely marginalized by history's relegation of women's herbal wisdom to "old wives' tales" and witchcraft. Negligibly few women published serious medical works until recent

decades. Thus, this issue of *HerbalGram*, dedicated to the brilliant and beloved Fredi Kronenberg, PhD, who dedicated her life to the endeavor of botanical research, is especially important. And, it is a great honor, as medical doctors, herbalists, and midwives, who have made it our lifelong commitment to maintain the traditions of herbal healing in our lives and communities and bridge our traditional knowledge with the best of conventional medicine and science, to bring this special issue to you.

Together, we decided that addressing the following questions in a conversational format would bring a distilled essence of the power and importance of botanical medicines for women today.

I also commonly use botanicals and conventional therapies in conjunction with each other.

As herbalists and midwives who became MDs, do you still use herbal medicines in clinical practice? To what extent?

Aviva Romm: Despite nearly a decade of medical training, which certainly encouraged reaching for a prescription pad first, the herbalist in me remains alive and well! Herbal therapies, along with dietary and nutritional interventions and mind-body approaches, remain the mainstay of my practice as a physician. I continue to use botanical medicines in nearly 100% of my patients, and always use them preferentially over conventional pharmaceuticals whenever possible for many mild-to-moderate, acute, or even complex chronic conditions. The reality is, in most cases, with the exception of emergencies and oncology, or advanced chronic disease (and sometimes even then), botanical medicines are safer and carry fewer side effects. Many botanical medicines are as effective as conventional pharmaceuticals, can be cost-effective, and are ecologically sounder than pharmaceuticals. While we've seen numerous conventional medications recalled, black-boxed, or reconsidered when post-market surveillance or long-term human use revealed them to be much more harmful than initially anticipated, the track record of safety and efficacy of herbs as first-line therapies for many conditions remains largely reliable.

I also commonly use botanicals and conventional therapies in conjunction with each other. For example, if a patient has severe panic attacks brought on by air travel, her conventional anti-anxiety medication may be ideal for her next flight; however, for managing her daily anxiety, a combination of meditation, magnesium, rhodiola (*Rhodiola rosea*, Crassulaceae), and lemon balm (*Melissa officinalis*, Lamiaceae) may be my prescribed protocol.

Herbal therapies also remain my first choice for health in my personal life — from herbs and spices in my food to a relaxing evening tea, to supporting my immune system during cold and flu season, to healing during those times something more is needed.

Tieraona Low Dog: Herbs always have been an integral part of my life and my clinical practice, and that didn't change after receiving my medical degree. There is a definite time and place for modern, conventional medicine, and my deep desire to understand "when and what" to offer was a driving force for going to medical school. While some herbalist colleagues and friends thought that medical school might destroy or diminish my love of herbs, my medical training actually deepened my understanding and appreciation for them. Listening to a pathophysiology lecture about some disease would get me thinking about how certain plants could be beneficial. When urgent care providers prescribed antibiotics for viral infections in children, I talked with parents about elderberry (*Sambucus* spp., Adoxaceae) syrup or gave them a recipe for homemade thyme (*Thymus* spp., Lamiaceae)

Lemon balm *Melissa officinalis*
Photo ©2019 Steven Foster

syrup. I see many people living with stress, worry, fatigue, insomnia, and chronic pain. Conventional pharmaceuticals are not the answer for most of these problems, but I have a whole pharmacopeia of plants to draw from. I prescribe more botanicals and dietary supplements than pharmaceuticals, by far, as part of a broader approach to medicine that includes nutrition, mind-body medicine, and other lifestyle recommendations. Knowing when and how to use botanicals makes me a more effective clinician. That knowledge, that ability to weave the plants into my practice, is a gift.

Botanicals need not be a modality we turn to for treatment alone; they are an important part of daily support and health support for the common challenges humans face — a role that most pharmaceuticals do not fill.

What is the importance of today's practitioners' including botanical medicines as part of their clinical repertoire?

AR: Practitioners must consider a wide range of factors when prescribing: therapeutic efficacy, safety, a patient's severity of symptoms and risks on a spectrum of health and disease, patient preference for the types of treatments she uses, costs to the patient, costs to the health care system, and public health and ecological costs (for example, antibiotic resistance or the presence of conventional pharmaceuticals as contaminants in waters, soil, and food). Our task as practitioners is to find the sweet spot among these various considerations. Botanical therapies often satisfy all of these parameters, and, as such, they provide us with the best medicine for helping our patients to heal. Further, botanicals need not be a modality we turn to for treatment alone; they are an important part of daily support and health support for the common challenges humans face — a role that most pharmaceuticals do not fill.

TLD: While conventional medicine was born out of an acute-care model of trauma and infectious disease, most of the problems we are dealing with today are the result of our modern lifestyle. We are drowning in a tsunami of obesity, diabetes, cardiovascular disease, stroke, cancer, depression, anxiety, and chronic pain. The primary approach is disease management via pharmaceuticals. While early detection is an important part of conventional care, when it comes to prevention and general health promotion, it is all lip service. There remains very little focus in medical training on nutrition, dietary supplements, mind-body therapies, or strategies for empowering people to take a more active role in their own care. Without question, botanicals have a place within this broader, integrative approach to health.

Many people with stress, worry, irritability, and fatigue do not meet the criteria for prescription antidepressants or anxiolytics, and the data are not compelling, at least for antidepressants, that they are effective for those with milder forms of depression. However, there are many herbs with a long history of use and varying levels of modern research to support their consideration for these individuals. Chamomile (*Matricaria chamomilla* syn. *M. recutita*, Asteraceae) flowers, lemon balm, passionflower (*Passiflora incarnata*, Passifloraceae), valerian (*Valeriana officinalis*, Caprifoliaceae), ashwagandha (*Withania somnifera*, Solanaceae), eleuthero (*Eleutherococcus senticosus*, Araliaceae), rhodiola, and skullcap (*Scutellaria lateriflora*, Lamiaceae) are a few that rise to the top of the list.

The opioid epidemic is real. Human suffering, both physical and emotional, is real. Pain is a vicious cycle that leads to disrupted sleep, depressed mood, anticipatory anxiety, hypersensitivity, and diminished quality of life. Botanicals can be used to address many of these issues as well. Turmeric (*Curcuma longa*, Zingiberaceae), boswellia (*Boswellia serrata*, Burseraceae), devil's claw (*Harpagophytum procumbens* and *H. zeyheri*, Pedaliaceae), corydalis (*Corydalis* spp., Papaveraceae), cannabis (*Cannabis sativa*, Cannabaceae), cramp bark (*Viburnum opulus*, Adoxaceae), kava (*Piper methysticum*, Piperaceae), ashwagandha, California poppy (*Eschscholzia californica*, Papaveraceae), and others can act as muscle relaxants, anti-inflammatories, analgesics, anxiety reducers, and/or mood boosters. Plants have multi-modal effects in the body. Unlike single-compound drugs, botanicals have an array of constituents that have the potential to interact with a wide range of cellular receptors. As part of an integrative strategy, plants can help our body regain its equilibrium.

What concerns, if any, do you have about the current state of herbal research or the herbal industry in general?

AR: While the number of studies on herbal therapies has increased tremendously over the past two decades, which is exciting, quality studies are, unfortunately, few and far between. This leaves many practitioners to base our herbal recommendations on a combination of best available evidence, traditional use, and trusted professional opinions — or, understandably, to toss our hands up, confused. A limited number of botanicals are backed by high-quality studies; too often, the studies we see are poorly designed, lack adequate power, and don't disclose enough product information, making them unreliable, clinically unhelpful, and of dubious relevance. I often find myself discarding research that comes across my desk.

Unfortunately, many manufacturers and most "online experts" in wellness and herbal medicine lack the training it takes to discern the value of published research. When these sources promulgate half-truths, exaggerated claims, and misinformation, practitioners and consumers alike are left confused and reliant on products that can be costly and ineffective. False product claims are rampant on the internet and are associated with a range of products, from those used for skin care to hormone therapy to cancer treatment. Training and information dissemination standards are needed at all levels of the wellness, botanical medicine, and supplements industry to ensure that the end user is able

to obtain both information and products that are reliable. Of course, this also means that better research is needed — and thus quality botanical research needs to be a priority at high-level institutions.

> Pain is a vicious cycle that leads to disrupted sleep, depressed mood, anticipatory anxiety, hypersensitivity, and diminished quality of life. Botanicals can be used to address many of these issues as well.

TLD: As a scientist and clinician, I am, of course, a strong advocate of well-done botanical research. While more rigorous studies are being conducted, solid research is still rather scarce in our field. In clinical trials, the herb used to address a specific problem is often poorly chosen, inappropriately dosed, or so poorly described that you have no real idea what was used. The results of a low-quality study are relatively meaningless, though this doesn't stop believers from citing them as proof that an herb "works," or critics from using them to say the herb is "worthless." Because herbal research often is delivered in media soundbites by those with no familiarity with the complexities of the topic, misreporting is commonplace and contributes to the confusion around the safe and appropriate use of herbal medicines.

As far as the herbal industry is concerned, many companies make good products, but the fact that adulteration still exists is just inexcusable. In addition to legitimate concerns about quality, the sheer number of products in the marketplace is frankly overwhelming. Sorting through products with widely varying dose ranges, herbal combinations, and vague, sometimes outrageous claims, is a highly confusing experience for most consumers. I've been involved in practitioner education for more than two decades and can honestly say that even with training, many health care professionals report feeling overwhelmed when standing in the

Passionflower *Passiflora incarnata*
Photo ©2019 Steven Foster

Cramp bark *Viburnum opulus*
Photo ©2019 Steven Foster

supplement aisle. An authoritative, easily accessible, scientifically based database that is free and understandable to the public could help people make informed decisions. Policymakers can look to Europe and Canada for other ways of addressing what claims can be made on the label to help consumers make informed decisions at the point of purchase.

When I prescribe a medicine to a patient with a medical condition, whether it be a conventional pharmaceutical or a botanical, I like to know that I can rely on its efficacy.

How can practitioners determine which herbal products to recommend to patients?

AR: This is one of the most common questions I receive from practitioners, and perhaps the most difficult to answer, because so many companies and products are on the market right now. While products must conform to a general set of quality and safety standards, there is still a tremendous amount of variability in raw materials and manufacturing practices, which ultimately determine the quality and efficacy of the medicine. When I prescribe a medicine to a patient with a medical condition, whether it be a conventional pharmaceutical or a botanical, I like to know that I can rely on its efficacy — which means it has to contain the ingredients that I am depending on for effects and outcomes, and should not contain unintended ingredients (contaminants), or intended but undeclared ingredients (adulterants). Yet in the current market, neither is guaranteed, and this is indeed a challenge. I therefore generally recommend companies that were created and are run by respected herbalists, as there is generally a higher level of respect for the need for raw material quality, and companies with high-quality assurance standards. I also recommend using products only from companies large enough to comply with Good Manufacturing Practices (GMPs),* and those that emphasize ecological practices and high-quality sourcing. Additionally, I recommend, when possible, using companies that are members of the American Herbal Products Association. I also concur with Dr. Low Dog on the additional steps you can take, as described below.

TLD: This is tough to answer, given everything that I've already mentioned. Clinicians can use extracts or products that have been studied in clinical trials. The fact that it was used in research gives clinicians a level of confidence in the quality and safety of the product, as well as in their dosing recommendations. However, most clinicians are unaware of which products have been used in clinical research. This is made worse by the fact that continuing medical education (CME) granting bodies do not allow speakers to mention commercial product names; they specifically ask that "generic" names be used. While this works for conventional pharmaceuticals, it is simply ludicrous when discussing herbal research. Talking about a study on "rhodiola" tells you nothing about the species, the part used, solvent, native extract ratio, etc. One helpful tip for clinicians is that those who have access to Natural Medicines Database can view the brand names of herbs and extracts that have been studied in clinical trials under the specific botanical monograph.

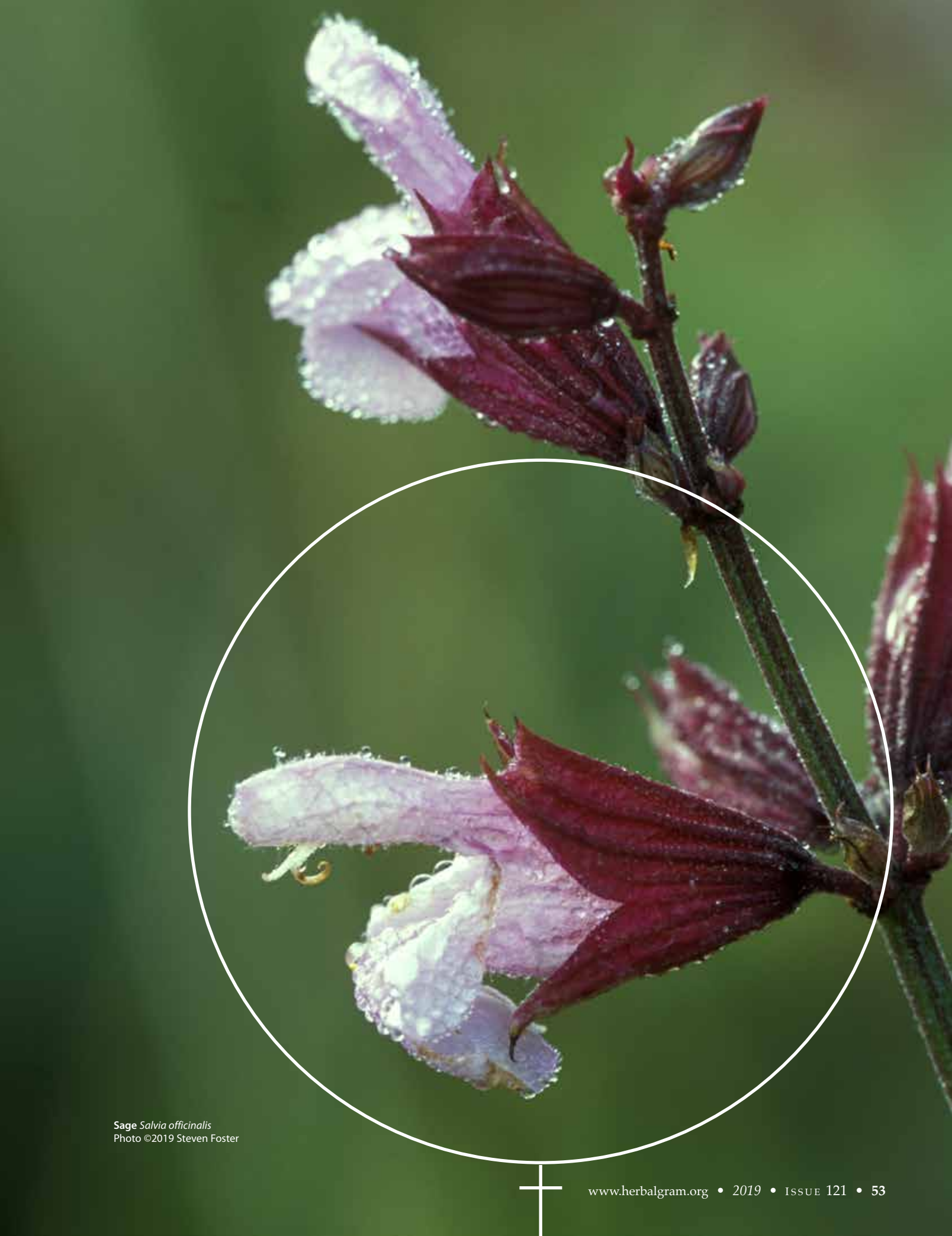
Some companies have United States Pharmacopeia (USP) or NSF quality seals on their labels, another good indicator of quality, but this is not common for most botanical products. Clinicians can talk directly with companies and ask questions about their quality control and check the FDA website to see if any warning letters have been issued. Practitioners can also talk with local retailers and ask what quality processes they have in place for the supplements they sell. Some, like Pharmaca, have a very lengthy application process for companies to sell products in their stores.

Do you see herbs as "green" allopathic substitutes/alternatives, or do they hold additional meaning and value to you?

AR: I do think plants have a role as green pharmaceuticals. I often use botanicals for specific therapeutic effects based on their pharmacologic actions in place of conventional pharmaceuticals, whether it is pyrrolizidine alkaloid (PA)-free petasites (*Petasites* spp., Asteraceae) root extract for migraines or lavender (*Lavandula* spp., Lamiaceae) oil for anxiety. But botanical medicines have the potential, for the curious and open-minded practitioner and patient, to serve as more — they can be a powerful, beautiful, meaningful bridge to connect with the innate healing power of nature, and, in doing so, with our own intrinsic healing capacities. When I prescribe a botanical remedy to a patient, it is usually a plant I have encountered — in my garden, in the woods, along a creek, roadside, or mountain hike — and I know the plant's habitat, growth habits, resilience, and beauty. My garden has served as an opportunity to introduce patients to the plant remedies I have prescribed them — the chamomile or lemon balm they will later use in their sleep remedy, the echinacea (*Echinacea* spp., Asteraceae) in their tincture for a cold, or the ashwagandha in their adaptogen blend — and it is eye-opening for them, as most of us think of medicines as inaccessible, sterile, laboratory-manufactured products. It can inspire a whole new respect for the planet and a desire to protect natural places.

Plants also have been used ceremonially throughout the world and across cultures — from incense in India or a Catholic church to burning spices at the close of the Sabbath in Jewish tradition, or burning sage (*Salvia officinalis*, Lamiaceae) and cedar (*Juniperus* spp., Cupressaceae) in a sweat lodge — they can be part of the connection we make, if we allow it, between ourselves and whatever you consider spirit in your life. Rituals can have a profound

* Legally, all herbal companies that produce dietary supplements are required to follow federally mandated GMPs, but individual herbalists may produce small-batch local products outside of these guidelines. Romm believes that it is not advisable to use these clinically.



Sage *Salvia officinalis*
Photo ©2019 Steven Foster

role in slowing down, going within, healing, and tapping into innate body wisdom. Plants play a role in my life every day, and each time I connect with one of these healers in nature, I am reminded that I am part of all of this beautiful creation — not separate from it — and that there is great wisdom in nature, in my body, and in each of my patients.

Plants play a role in my life every day, and each time I connect with one of these healers in nature, I am reminded that I am part of all of this beautiful creation — not separate from it — and that there is great wisdom in nature, in my body, and in each of my patients.

TLD: Plants often do represent a safer, greener alternative to a pharmaceutical drug. That's important in and of itself. But that's not all there is. There is something about using herbal medicine that's missing with pharmaceuticals: connection. One day as a medical student, after seeing a patient with strep throat, my attending physician asked me to write a prescription for amoxicillin. As I sat looking at the blank prescription form, he asked if I needed help. I said no but then asked, "How exactly is amoxicillin made? Where does it come from? From a fungus, like penicillin?" The attending physician said he didn't know and then asked why it mattered. I told him, "I've never given anybody a medicine I didn't make myself. It feels strange."

You see, I'd been gathering and growing plants and making them into teas, tinctures, syrups, and salves for years. I tasted them. I used them. I gave them to my babies. I gave them to hundreds and hundreds of people and learned what did and didn't work. I used them in clinic. I used them in ritual. I had my own personal experience with them, not just from reading books or listening to experts, but from directly interacting with them. I've wandered the deserts, forests, and mountains of New Mexico for decades looking for medicine. And I found it everywhere. I learned where the plants lived. I learned how to use their gifts. I learned their stories.

So, is there something deeper? Definitely. HG

Butterbur *Petasites* spp.
Photo ©2019 Steven Foster

***Aviva Romm, MD, and Tieraona Low Dog, MD, are long-time members of the American Botanical Council (ABC) Advisory Board. The views expressed in this Q&A are their own and do not necessarily reflect those of ABC and* HerbalGram.**

Aviva Romm, MD, *is a midwife, herbalist, and Yale-trained MD, board certified in family medicine with obstetrics, who has been bridging what she considers the best of traditional medicine with good science for more than three decades. She focuses on identifying and reversing the root causes of chronic health conditions in women's, maternal, and pediatric health. She is considered a leader in botanical medicine and is the author of seven books on natural medicine, including the textbook* Botanical Medicine for Women's Health *(Elsevier), which won the 2010 ABC James A. Duke Excellence in Botanical Literature Award, and* The Adrenal Thyroid Revolution *(Harper One). She is also a co-author of* The American Herbal Products Association's Botanical Safety Handbook, *2nd edition (CRC Press). For more than a decade, Romm served as both the president of the American Herbalists Guild and medical director of the American Herbal Pharmacopoeia, and as a botanical industry consultant. She is the co-founder of the*

So, is there something deeper? Definitely.

Yale Integrative Medicine Curriculum. Romm lives and practices medicine in the Berkshires and New York City, respectively.

Tieraona Low Dog, MD, *is a physician, author, and thought leader in integrative medicine. Her background in herbal medicine, midwifery, massage, and martial arts made her a natural choice to lead the fellowship program at the University of Arizona Center for Integrative Medicine, where she oversaw the training of more than 600 physicians and nurse practitioners. Low Dog is one of the nation's foremost experts in dietary supplements and botanical medicine, and has been honored with many awards from academia, public health, and industry throughout her 40-year career. A prolific scholar, she has authored or co-authored 52 peer-reviewed journal articles, 22 chapters for medical textbooks, and five books, including four with* National Geographic*; and was co-editor of* Integrative Women's Health *(Oxford University Press). She has chaired expert panels for supplement/botanical safety at the United States Pharmacopeia, including joint reviews with the Department of Defense, for the past 20 years. Low Dog has been an invited speaker at more than 600 conferences, reaching more than 50,000 people every year with her message of integrative medicine, compassionate care, and deep ecology. She lives and practices outside of Santa Fe, New Mexico.*

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California poppy *Eschscholzia californica*
Photo ©2019 Steven Foster

Fredi Kronenberg in 2010
Photo courtesy of Steven Foster

FREDI KRONENBERG

An Enthusiastic Scientist and Faithful Friend

By Adriane Fugh-Berman, MD, and Christine Wade, MPH

"Through many exciting years, our deep friendships with Fredi developed and endured, and made working with her multi-dimensional, meaningful, and fun. We know that many of Fredi's collaborators felt the same way and continue to miss her."

Fredi Kronenberg, PhD, was an energetic and enthusiastic scientist who combined an insatiable curiosity with a rigorous commitment to carefully analyzing data and documenting research findings. She applied her brilliant scientific mind on both a macro and micro level to the world, daily living, and her own health. She was curious about everything, especially the natural world, people, and relationships. We remember her talking about passing a dead pigeon on a sidewalk she traversed daily and watching it decay over time, and how it metamorphosed from bird to soil. "It was so interesting," she said. "I wish I had taken a picture of how it changed day to day." Fredi made the comment with deep reverence intertwined with an intense desire to understand life in its many phases. She applied the same reverence and curiosity when it came time for her to explore her own transition from life to death.

Fredi received a bachelor's degree from Cornell University and a doctorate from Stanford University, where she focused on thermoregulatory physiology. Her first subjects were honeybees (she painstakingly caught them and inserted a thin wire thermometer on their bodies), and descendants of her initial colony still thrive on Stanford's campus. But it was the rhythms of women that captivated her and to which she turned her professional attention as a post-doc at Columbia University's College of Physicians and Surgeons. She became a groundbreaking investigator on the physiology of hot flashes, and her work helped establish the scientific study of menopause. She subsequently co-founded the North American Menopause Society.

Fredi was fascinated by not only the mechanisms underlying hot flashes but also how women experienced them. While sympathetic to women whose hot flashes were highly disruptive, Fredi also reported physiological hot flashes in women who were unaware they were having them. Fredi believed that many women's health conditions are overtreated, while others are neglected. With respectful curiosity, she listened to the women who generously gave their time to her studies, while hooking them up to all sorts of

monitors in her basement lab at Columbia. She asked persistent questions, and she was so personable that these women were always eager to talk with her, so she learned about all they were doing to manage their annoying and sometimes debilitating symptoms.

Fredi's scope extended beyond hot flashes to general women's health throughout various life stages, from menarche, to mid-life, to menopause. She was especially interested in women's health care choices and the lack of treatment options in some areas. With a team of collaborators across Columbia's medical school and school of public health, she conducted the first large-scale national survey of women's health conditions, in four languages, which provided the first estimates of choices made by women of color in the United States. Women were asked about how they sought health care, which remedies they used at home, and which strategies they disclosed to, or hid from, their health care providers. It was because of women's experiences, stories, and desire for more treatment options that Fredi's interest in botanical medicine grew and became a focus of her work.

The 1990s were a heady time for so-called "alternative medicine." Fredi was in the thick of it, always providing an open-minded but scientific perspective, even in settings where belief in magic often outshouted pleas for unbiased scientific investigation.

The 1990s were a heady time for so-called "alternative medicine." Fredi was in the thick of it, always providing an open-minded but scientific perspective, even in settings where belief in magic often outshouted pleas for unbiased scientific investigation. Fredi always had a scientific perspective but also firmly respected traditional medicine systems and traditional healers from cultures around the globe as a source of knowledge and ideas to be further investigated. In 1993, using this blend of perspectives and a donor gift, Fredi co-founded the Richard and Hinda Rosenthal Center for Complementary & Alternative Medicine at Columbia University, which was the first of such academic research centers at an Ivy League university. Soon after its founding, the Rosenthal Center became a National Institutes of Health (NIH)-funded research center. She forged through ensuing controversies with an amenable attitude toward naysayers, while insisting on the legitimacy of groundbreaking research questions. She wanted to know every possible thing and thought that every detail was relevant to larger questions. She often stubbornly challenged conventional wisdom if it did not support her observations, and she often was proved right.

But Fredi's legacy didn't stop there. She was a founding editor of *The Journal of Alternative and Complementary Medicine: Research on Paradigm, Practice and Policy*. She was also a founder of the Consortium of Academic Health Centers for Integrative Medicine. Her annual continuing medical education conference at Columbia, "Botanical Medicine in Modern Clinical Practice," which ran from 1996 to 2005, brought together leading voices in botanical medicine and attracted hundreds of physicians and other health care providers, who incorporated what they learned about botanical medicine into their practices. She also produced an "Integrative Pain Medicine" course to educate physicians on non-pharmaceutical approaches to pain management. Fredi then expanded into food and medicine, collaborating closely with Andrew Weil, MD, on "Nutrition & Health: State of the Science," a continuing medical education course at the University of Arizona. More recently, as a visiting research scientist at Stanford, Fredi questioned the nutritional content of hospital food and persuaded Stanford to hold a conference that focused on the role of diet in healing and recovery.

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From a young age, Fredi documented everything. Her sense of wonder for the natural world, keen observation skills, and appetite for varied experiences made her a skilled photographer. Her hundreds of fine photographs of healers and patients from around the world are outnumbered only by her images of plants and critters in the many international settings to which she traveled, from India, China, and Japan, to Costa Rica, Belize, and South Africa.

Fredi kept personal health records for decades, including in her last years of life as she documented her illness. Her creativity and inventiveness extended to the smallest of tribulations. She was taking so many pills they wouldn't fit into a regular pill container, so she used the edge of an iron to heat-seal and compartmentalize Ziploc sandwich bags into three-compartment pill-holders. A scientist to the end, when she was taking a medication that could cause voice changes, she recorded her voice regularly to see if its pitch changed. As her lung function declined because of the lung cancer that eventually led to her death, Fredi recorded changes in blood oxygen levels with a pulse oximeter, testing variations during exertion or rest.

She researched everything about her disease: the etiology; conventional treatments; alternative treatments; lung transplants; the best, most discreet oxygen tanks; the most un-hospital-gown-like hospital apparel. She loved the many caring health care practitioners, some of whom were oncologists and others who were traditional Chinese medicine practitioners, who helped her with the many tough medical decisions she faced after a diagnosis of Stage IV lung cancer, even though she was not a tobacco (*Nicotiana* spp., Solanaceae) smoker. She lived with the condition for more than 10 years, an astounding amount of time for such a poor prognosis. When she ascertained that she was at a stage where no evidence supported one treatment over another, she came up with research questions that she hoped others would answer. She never lost her scientific perspective.

When she ascertained that she was at a stage where no evidence supported one treatment over another, she came up with research questions that she hoped others would answer. She never lost her scientific perspective.

Fredi made friends easily, focusing her empathetic attention in a way that made someone feel like they were the only person in the world. She was as endlessly curious about people's lives as she was about, well, rotting pigeons. Fredi acted like she had all the time in the world — a problem when colleagues wanted to actually finish something — but it made her a great friend.

Fredi didn't want colleagues to know about her lung cancer, because she didn't want to be pitied, and she didn't want her identity to be reduced to that of a patient. We believe that many people at her 60th birthday party knew about her illness; it was a joyful event, but layered with our collective, painful consciousness that our time with her would be truncated. Wonderful tributes to her from the amazing variety of friends Fredi cultivated were full of heartfelt gratitude and laughter. We sang a cover of "Times They Are A'Changing" — with lyrics about bees and NIH grant deadlines. Fredi loved singing, guitars, and banjos.

Fredi was herself to the end. After all the treatments, when there was nothing more to do, even when she was hours from death, she hated to talk about dying. It's not that she was afraid of death — in fact, she was curious about it. It's that she didn't want to be dying on her way to death. With whatever time she had left, Fredi wanted to live, not die. That was Fredi. Full of life, full of curiosity, loving, optimistic, enthusiastic. She will be in our hearts always. HG

Christine Wade with Fredi Kronenberg.
Photo courtesy of Christine Wade.

***Adriane Fugh-Berman, MD**, is a professor in the department of pharmacology and physiology and the department of family medicine at Georgetown University Medical Center, where she directs Urban Herbs, an ecological gardening project, directs PharmedOut, a project that fosters rational prescribing, and codirects a Master of Science (MS) program in Health and the Public Interest. She worked with Fredi as a writer, educator, and researcher.*

***Christine Wade, MPH**, is the former associate director of the Rosenthal Center for Complementary & Alternative Medicine at Columbia University's College of Physicians and Surgeons. She is working on her second novel, a medical mystery. She wrote her first,* Seven Locks *(Simon & Schuster, 2013), after the Rosenthal Center closed in 2007.*

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A Botanical Approach to Symptom Management During and After Breast Cancer Treatment

By Lise Alschuler, ND, FABNO

Breast cancer is the most common cancer in the United States, with 266,120 cases in women and 2,550 cases in men diagnosed in 2018.[1] In women, breast cancer represents 30% of all cancers diagnosed and is responsible for 14% of all deaths from cancer.[2] Of all breast cancers diagnosed in women, more than three-quarters are diagnosed in postmenopausal women.[3] The five-year survival rate for localized breast cancer is 99%, whereas the five-year survival for metastatic breast cancer is 27%.[4] According to the American Cancer Society, deaths from breast cancer in the United States have fallen by 30% over the past two decades.[5] This improvement is likely due in part to better screening, which results in an increased proportion of early stage diagnoses that are more amenable to treatment. Improved treatments also have contributed to this favorable trend. The majority of women diagnosed with breast cancer will undergo conventional treatment in the form of surgery, radiation, chemotherapy, and/or endocrine therapy. Many of these women seek additional integrative therapies, including botanicals, to improve their tolerance to, and the efficacy of, these conventional treatments.

While the clinical data supporting the use of botanicals concurrent with conventional treatment is far from robust, there is a body of emerging data. One area of interest is the reduction of adverse side effects, which can make conventional treatment a more tolerable experience and improve treatment adherence, thereby supporting better outcomes. This article provides an overview of the current state of evidence for selected botanicals for improving outcomes with conventional therapies.

An Integrative Approach for Women with Breast Cancer

Breast cancer is a potentially life-threatening disease, and the conventional treatments in use are effective for most women. Adjunctive integrative therapies that support a woman's well-being, while complementing and not interfering with conventional treatment efficacy or safety, may be valuable.[6] Safe, concurrent integrative botanical therapy requires nuanced knowledge of the type of breast cancer diagnosis and the conventional treatment(s) being used. For each chemotherapeutic agent, molecular targeted therapy, immune therapy, and endocrine therapy, it is important to know the class of drug, mechanism(s) of action, metabolism and terminal half-life, schedule of treatments, intent of the treatment (curative or palliative), and how each botanical or other integrative therapy might interact or interfere. For radiation therapy, the type and duration of treatment as well as the type and location of tissues within the radiation field should be ascertained in order to accurately anticipate the nature and location of potential radiation toxicities, which, in turn, can inform botanical recommendations.

It is equally important to have strong knowledge of the botanicals intended for use in a patient with breast cancer undergoing conventional treatment. Phytochemical constituents have the potential to interfere with drug metabolism, drug mechanisms of action, and/or the effects of radiation and, therefore, may modulate efficacy or increase toxicities. Botanicals may be counterproductive when used in conjunction with certain conventional treatments. For instance, the use of herbs such as *dong quai* (*Angelica sinensis*, Apiaceae)[7] and fenugreek (*Trigonella foenum-graecum*, Fabaceae) seed husks[8] that may potentially raise estradiol levels or stimulate estrogen receptor-mediated cell growth would be contraindicated during hormonal treatment with aromatase inhibitors. In addition, herbs that may have antiplatelet or anticoagulant effects, such as *dan shen* (*Salvia miltiorrhiza*, Lamiaceae),[9] should be used judiciously in patients with low platelet counts (less than 25,000), a relatively common effect of certain chemotherapeutics and found in some women with advanced disease. Finally, choosing high-quality botanicals is of utmost importance in order to avoid the introduction of potential adulterants, contaminants, excessive extraction residues, or other compounds with potentially toxic effects.

Turmeric *Curcuma longa*
Photo ©2019 Steven Foster

The primary focus of this discussion of herbal medicine in integrative oncology is to mitigate symptoms during conventional treatment. Given the lethality of cancer, it is essential to use an evidence-informed treatment approach. While the evidence base for botanicals in this regard is small, women are asking questions about the use of botanicals, and clinicians should be aware of the evidence for specific herbs that may aid in symptom management during active conventional treatment.

Botanicals during Chemotherapy

Turmeric

Turmeric (*Curcuma longa*, Zingiberaceae) is a well-known herb with anti-inflammatory actions. Systemic inflammation underlies many cancer- and treatment-related symptoms and is also a risk factor for disease progression and poor outcomes.[10] A randomized, double-blind, placebo-controlled eight-week trial of 98 adults with solid tumors (primarily breast, colorectal, and gastric) assessed the impact of curcumin supplementation on systemic inflammation.[11] The intervention was 300 mg phytosomal curcumin (Meriva; Indena SpA; Milan, Italy) three times daily, providing 180 mg curcuminoids daily. Chemotherapy regimens that were commonly used for these cancers were docetaxel-cisplatin-5-fluorouracil (5-FU) (gastric cancer and breast cancer), topotecan-cyclophosphamide-etoposide (breast cancer), cyclophosphamide-methotrexate-5-FU (breast cancer), and 5-FU-based regimens (colorectal cancer). Curcumin supplementation resulted in significantly greater improvements in quality of life (QoL) after eight weeks compared with placebo ($P < 0.001$). Additionally, various biomarkers of systemic inflammation reduced significantly in the curcumin group, including tumor necrosis factor-alpha (TNF-α), transforming growth factor-beta

American ginseng *Panax quinquefolius*
Photo ©2019 Steven Foster

(TGF-β), high-sensitivity C-reactive protein (hs-CRP), and calcitonin gene-related peptide (CGRP). The phytosomal, or liposomal, form of curcumin used in this trial may minimize the risk of herb-drug interactions, as compared to turmeric/curcumin products containing piperine (an alkaloid derived from black pepper [*Piper nigrum*, Piperaceae]).[12]

Capecitabine, another commonly used chemotherapeutic, is associated with a 40% to 50% incidence of hand-foot syndrome (HFS), a form of peripheral neuropathy. In a six-week pilot study of 40 patients (80% were female and 52% had breast cancer) receiving capecitabine, 4 g of turmeric (95% curcumin extract), taken as two capsules 12 hours apart, was associated with a reduced incidence of all grades of HFS, specifically 27.5% incidence after the first cycle of capecitabine treatment and 34% after the second cycle. The incidence of grade 2 or higher HFS (more severe) was only 10% after the first and second cycles of capecitabine, as compared to observed rates of 29% to 38% in placebo groups reported in other trials.[13] While these data are encouraging, this study is limited by its small size and the lack of a control group.

American Ginseng

Patients undergoing chemotherapy often experience fatigue. American ginseng (*Panax quinquefolius*, Araliaceae) is reputed to have anti-fatigue effects and has been a botanical of interest for this purpose. An eight-week, placebo-controlled clinical trial randomly assigned 364 adults actively receiving, or having recently completed, curative-intent treatment for cancer (all cancers were included except brain or central nervous system lymphoma) to 2 g American ginseng root extract (3% ginsenosides) or placebo daily to assess effects on fatigue.[14] Compared to the placebo group, ginseng supplementation was associated with a significant improvement in fatigue after eight weeks of treatment ($P = 0.003$). A subgroup analysis comparing patients undergoing treatment versus those who had completed treatment found significant improvements in fatigue at both four weeks ($P = 0.02$) and eight weeks ($P = 0.01$) in the ginseng patients undergoing treatment, compared to those undergoing treatment in the placebo group.

American ginseng has been shown to downregulate inflammation and modulate cortisol levels in stressed individuals, which may explain its potential benefit in fatigued patients. American ginseng does not have significant effects on cytochrome P450 enzymes, according to an in vitro assay, though further study is required.[15] Furthermore, water-extracted American ginseng and the crude root have not been shown to have estrogenic properties,[16] and in vitro data suggest American ginseng may have an inhibitory effect on the growth of breast cancer cells.[17] While these results need to be replicated in other studies, given the lack of any pharmacologic treatments for cancer-related fatigue, and the low risk presented by *P. quinquefolius*, this herb may be a reasonable option for patients.

Valerian

Sleep disruption is common among patients undergoing conventional cancer treatment, particularly chemotherapy. Poor sleep contributes to fatigue and reduced QoL during treatment. Valerian (*Valeriana officinalis*, Caprifoliaceae) root was studied in a phase III randomized, placebo-controlled trial of 227 patients undergoing

Valerian *Valeriana officinalis*
Photo ©2019 Steven Foster

cancer treatment who had difficulty sleeping.[18] More than 66% of participants had breast cancer and were receiving chemotherapy. The subjects were randomly assigned to receive 450 mg valerian root standardized to 0.8% valerenic acid or placebo one hour before bedtime each day for eight weeks. The Pittsburgh Sleep Quality Index (PSQI) and other sleep-quality questionnaires were used to evaluate response. While there was no significant improvement in overall sleep quality in the valerian group, the investigators reported improvements in several secondary outcomes including fatigue, sleep latency, amount of sleep per night, and drowsiness. However, these findings also lacked statistical validity. There were no serious toxicities reported. It should be noted that most studies of valerian root for insomnia use 450-900 mg of an ethanolic extract of valerian with an herb-extract ratio of 4-7:1. The use of 450 mg crude valerian root powder in this study is on the low end of typical doses.

Although there are several preclinical studies that demonstrate valerian's effect on various cytochrome P450 enzymes, clinical studies have failed to find any relevant interactions with anticancer drugs.[19] There seems to be no evidence that valerian raises serum estrogen levels or has significant stimulatory effects on the estrogen receptor.

Ginger

Clinical studies have yielded varying results for the antiemetic effect of ginger (*Zingiber officinale*, Zingiberaceae) on chemotherapy-induced nausea.[20] One positive trial was a double-blind, multisite prospective clinical study that included 744 participants with various types of cancer (74% breast cancer) receiving chemotherapy.[21] The subjects were assigned to either placebo or to one of three different daily doses of ginger: 0.5 g, 1 g, or 1.5 g. All subjects took the treatment for six days beginning three days prior to the start of each chemotherapy treatment. All patients also received an antiemetic (5-HT_3 receptor antagonist) and dexamethasone (a steroid) with each chemotherapy cycle. While all doses of ginger reduced nausea compared to placebo on the first day of chemotherapy (P = 0.003 overall), the two smallest doses (0.5 g and 1 g) reduced nausea the most (P = 0.017 and P = 0.036, respectively).

Ginger is purported to have antithrombotic actions at high doses, although in a systematic review, the majority of studies did not find an inhibitory effect on platelet aggregation at the 3.6-5 g dosage range.[20] Caution may be warranted with the concurrent use of ginger and chemotherapeutics metabolized by cytochrome P2C9 or cytochrome P3A4, as ginger has been shown to inhibit these enzymes in vitro.[22] The rapid half-life of key compounds in ginger may, however, mitigate the risk of herb-drug interactions.

Botanicals during Endocrine Therapy

Black Cohosh

Hot flashes are a common symptom in women taking endocrine therapies (tamoxifen citrate, anas-

Ginger *Zingiber officinale*
Photo ©2019 Steven Foster

trozole, exemestane, letrozole, and fulvestrant). Since the aim of endocrine therapy is to lower estrogen levels, the use of estrogenic substances is ill-advised. Numerous studies have evaluated the effects of black cohosh (*Actaea racemosa*, Ranunculaceae) for menopausal hot flashes, making it an herb of interest for patients and clinicians. Black cohosh does not contain phytoestrogens and does not stimulate the estrogen receptor.[23] In fact, some research suggests that black cohosh may inhibit the proliferation of estrogen receptor-positive (and estrogen receptor-negative) breast cancer cells.[24] Though clinical trials on black cohosh for hot flashes are mixed, the plant might be helpful for some women. The effect on hot flashes appears to be due to the impact of various plant components acting on the central endogenous opioid system[25] and the hypothalamus with dopaminergic, noradrenergic, serotoninergic, and GABAergic effects.[26]

In a study of 136 women taking tamoxifen (20 mg daily), a majority of the 90 patients who also took a black cohosh extract (Klimadynon, now sold as Monopret; Bionorica AG; Neumarkt, Germany; a 10:1 58% ethanol extract yielding 2.8 mg proprietary extractant) had reduced hot flashes after the intervention.[27] Specifically, after 12 months of 20 mg Klimadynon daily, 50% were free of hot flashes compared to only 26% in the tamoxifen-only group. In addition, only 25% of the women who took black cohosh extract experienced severe hot flashes. No serious adverse events were reported. The study was limited by the fact that it was open-label, there was no placebo arm, and there were twice as many women in the tamoxifen-plus-black cohosh extract group than in the tamoxifen-only group.

In addition to its potential benefit in reducing hot flashes, black cohosh may be associated with reduced risk of breast cancer recurrence. In an observational retrospective cohort study of 1,102 women previously diagnosed with breast cancer and taking tamoxifen, the use of black cohosh was associated with a 17% reduced risk of recurrence.[28] Another retrospective study of 949 patients with breast cancer and 1,524 controls found that the use of black cohosh was associated with a 53% reduced risk of recurrent breast cancer.[29]

Black cohosh has no known clinically relevant effects on cytochrome P450 enzymes,[30] or any known hepatotoxic effects. However, there have been some reported cases of hepatotoxicity associated with black cohosh dietary supplement products. A United States Pharmacopeia review in 2010 recommended a caution label on black cohosh products, but a subsequent examination of these cases suggested that the hepatotoxicity might be the result of quality problems, likely adulteration with other *Cimicifuga* species, and that black cohosh itself does not appear to pose a risk of hepatoxicity.[31,32] A 2018 study found that, when tested, only seven of 36 (19%) commercial black cohosh products contained true *Actaea racemosa*; the other 29 products indicated adulteration.[33] Clinicians should be aware of the quality issues surrounding black cohosh in the marketplace and counsel women appropriately.

Black cohosh *Actaea racemosa*
Photo ©2019 Steven Foster

Botanicals during Radiation Therapy

Calendula

One of the most common adverse effects associated with radiation therapy for breast cancer is radiation dermatitis. Radiation dermatitis is painful and, when severe, can interrupt radiotherapy. In a phase III non-blinded, randomized study of 254 patients with breast cancer receiving postoperative radiation therapy, application of topical calendula (*Calendula officinalis*, Asteraceae) ointment (Pommade au Calendula par Digestion; Boiron Ltd.; Messimy, France) to radiation-exposed skin resulted in 22% lower incidence of grade 2 or higher dermatitis compared to treatment with trolamine cream.[34] The subjects applied the ointments twice daily at least two hours before each radiation treatment.

However, in a larger randomized, double-blinded phase III study that compared the use of topical calendula (Calendula Weleda cream, 10% calendula; Weleda; Arlesheim, Switzerland) to an aqueous cream in 411 women with breast cancer undergoing radiation, no differences between the groups in patient-reported symptoms (pain, burning, itching, pulling, tenderness) were noted at any of the evaluation points. The incidence of severe acute radiation skin reactions of grade 2 or lower at the follow-up visit was 23% in the calendula group and 19% in the aqueous cream (placebo) group.[35] The cream was applied twice daily, and subjects were advised not to apply the cream within two hours of each radiation treatment.

Green Tea

Green tea (*Camellia sinensis*, Theaceae) preparations sometimes are used topically to minimize radiation dermatitis. Epigallocatechin gallate (EGCG), a key catechin in green tea, scavenges superoxide anions, hydroxyl radicals, and hydrogen peroxide, and can bind free radicals, protecting DNA from radiation-induced damage. This benefit was demonstrated in a single arm, prospective phase II clinical trial of 49 patients with breast cancer who received radiation therapy over four weeks.[36] All patients receiving radiation therapy began treatment when they developed grade 1 dermatitis. Treatment consisted of a solution of 660 mmol of 95% EGCG per liter saline sprayed onto the exposed skin three times daily. In this group of patients, the maximum grade of dermatitis over a mean duration of treatment of four weeks was mild (grade 1) in 71%, moderate (grade 2) in 29%, and no patients experienced more severe (grades 3-4) dermatitis. EGCG also improved dermatitis and improved pain in 85.7% of patients, burning in 89.8%, itching in 87.8%, and skin pulling in 71.4%. While this was an open study without a placebo arm, the results suggest that topical EGCG may limit the severity and symptoms of radiation dermatitis. The solution used

Calendula *Calendula officinalis*
Photo ©2019 Steven Foster

Green tea *Camellia sinensis*
Photo ©2019 Steven Foster

in this study can be approximated by mixing sufficient green tea standardized extract powder to obtain 350 mg EGCG with 1 liter of saline solution. The solution can then be sprayed onto skin with a nasal or throat mister.

Turmeric and Curcuminoids

Curcuminoids, the pigmented compounds found in turmeric rhizome, also have been studied for radiation dermatitis. In a randomized, double-blind, placebo-controlled trial of 30 patients with breast cancer receiving radiation therapy over four to seven weeks, 2 g turmeric containing 95% curcuminoids (Curcumin C3 Complex; Sabinsa; East Windsor, NJ) taken orally three times daily reduced the severity of radiation dermatitis at the end of treatment compared to placebo (radiation dermatitis scores of 2.6 vs. 3.4; $P = 0.008$).[37] Significantly, only 28.6% of the curcuminoid-treated patients developed moist desquamation (skin thinning and oozing as a result of radiation-induced damage to the epithelium) compared to 87.5% of the placebo-treated patients.

In addition to the potential protective effect of curcumin on the skin, there is in vitro evidence of a radiosensitizing effect from curcumin on breast cancer cells.[38] In spite of these positive results, a multisite double-blind, placebo-controlled trial of 686 patients with breast cancer failed to find benefit in the prevention of radiation dermatitis with 2 g of the previously mentioned turmeric product when taken orally three times daily over placebo throughout the course of radiation treatment plus one week after treatment.[39]

Mushrooms

Not a class of botanicals, mushrooms are in the kingdom Fungi. A proprietary processed liquid fermentation of the turkey tail mushroom (*Coriolus versicolor* or *Trametes versicolor*, Polyporaceae) known as Polysaccharide Krestin (PSK) has been shown in an adjuvant randomized trial of 914 women to increase disease-free survival in patients with node-negative, ER-negative, and stage IIA T2N1 breast cancer. The dose used in the study was 3 g per day.[40] Similar effects were observed in a randomized trial of 227 patients with operable breast cancer with vascular invasion of the tumor and/or of metastatic lymph nodes. The survival curve was improved in the group who took a daily dose of 3 g PSK concurrent with chemotherapy (5-FU, cyclophosphamide, mitomycin C, and prednisolone [FEMP]) compared to chemotherapy alone ($P = 0.0739$).[41]

The survival impact from the addition of *T. versicolor* to conventional treatment was assessed in a 2012 meta-analysis of 13 clinical trials with 2,587 subjects being treated for various solid tumors. Subjects with breast, gastric, or colorectal cancer who took *T. versicolor* extracts (PSK, PSP [Chinese product equivalent of PSK], and mycelium extracts were all included) typically dosed at 3 g daily had a 9% absolute five-year overall survival benefit, resulting in one additional patient alive after five years for every 11 patients treated with the mushroom.[42] There are no known herb-drug interactions with turkey tail mushroom.

Conclusion

Conventional breast cancer treatments offer women the most desirable disease outcomes, including, for many, remission. However, the treatments can be difficult to tolerate due to the many accompanying side effects. A broader integrative approach may optimize treatment tolerance and, therefore, success. Women are pursuing adjunctive therapies, including botanicals, while clinicians are faced with trying to provide evidence-informed counsel on their use. While the body of evidence supporting the inclusion of botanicals in integrative breast cancer care continues to expand, studies that evaluate the efficacy and impact of botanicals on the main outcome of conventional treatment are limited. Additionally, the content and quality of botanical supplements may vary, confounding conclusions from clinical trials. This state of evidence has led the Society for Integrative Oncology, in its 2018 guidelines on the use of integrative therapies during and after breast cancer treatment, to conclude that there is no strong evidence to support the use of ingested dietary supplements (including herbs) in the management of treatment-related toxicities.[43] Therefore, patients with cancer should only use these botanicals with the guidance of health care professionals. Future clinical efficacy studies may generate greater clarity on the specific indications for botanicals in the integrative treatment of breast cancer. HG

Turkey tail mushroom *Trametes versicolor*
Photo ©2019 AndrewC

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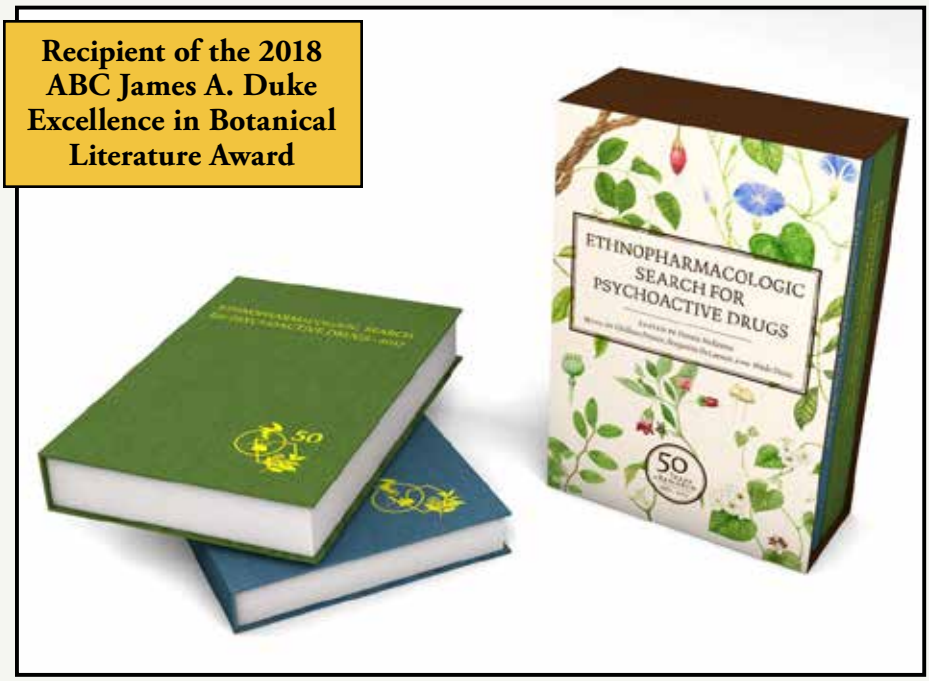
Recipient of the 2018 ABC James A. Duke Excellence in Botanical Literature Award



***Ethnopharmacologic Search for Psychoactive Drugs*, Volumes I and II,** by Dennis McKenna, ed. Santa Fe, NM: Synergetic Press; 2018. Hardcover, 832 pages. ISBN: 978-0907791-68-3. $125.00.

Ethnopharmacologic Search for Psychoactive Drugs is a two-volume compilation of 50 years of research on psychoactive plants and fungi. Volume one contains the proceedings of the first, groundbreaking Ethnopharmacologic Search for Psychoactive Drugs (ESPD) symposium held in 1967. Fifty years later, in 2017, the second ESPD symposium occurred, which covered developments and setbacks in the field during this interval. Volume two, which is the focus of this review, covers the proceedings of the 2017 ESPD symposium.

Prominent experts — including Kenneth Alper, MD; Evgenia Fotiou, PhD; Nigel Gericke, MD; Michael Heinrich, PhD; and Luis Eduardo Luna, PhD; among many others — are featured in this volume, along with individuals with career-long interests in the cultural use of mind-altering plants and fungi across the globe. The book topic likely attracts a wide audience, with greatest appeal to academics and what the text refers to as "underground researchers." The general public also would find interest in learning about the worldwide diversity of plants and fungi that alter consciousness.

Volume two is divided into four major sections: "Ayahuasca & the Amazon;" "Africa, Australia & Southeast Asia;" "Mexico & Central America;" and "Biosphere." The "Ayahuasca & the Amazon" section is well-represented, at nearly the length of the "Africa, Australia & Southeast Asia" section, possibly reflecting the editor's personal and professional experience, as well as the high diversity of plants native to the Amazon. The "Mexico and Central America" section is the shortest, and the "Biosphere" section includes shorter articles that are broad in scope.

The introduction, "What a Long, Strange Trip it's Been: Reflections on the Ethnopharmacologic Search for Psychoactive Drugs 1967-2017," provides a social and scientific context for the volume, beginning with a reflection of the psychoactive journey since the first ESPD conference in 1967 and followed by a deconstruction of the "hippie" movement in "A Scientist Looks at Hippies."

Within the "Ayahuasca & the Amazon" section, "Ayahuasca: A Powerful Epistemological Wildcard in a Complex, Fascinating and Dangerous World" provides an overview of ayahuasca (*Banisteriopsis caapi*, Malpighiaceae) brew as a traditional spiritual sacrament and a modern mind-altering medicine. "From Beer to Tobacco: A Probable Prehistory of *Ayahuasca* and *Yagé*" focuses on many aspects of ayahuasca brew and its admixtures, including those that contain tobacco (*Nicotiana* spp., Solanaceae). "Plant Use and Shamanic *Dietas* in Contemporary *Ayahuasca* Shamanism in Peru" is a personal ethnography of firsthand experience with Peruvian ayahuasca shamanism from the perspective of anthropologist Evgenia Fotiou. "Spiritual Bodies, Plant Teachers and Messenger Molecules in Amazonian Shamanism" explains fascinating shamanic rituals involving ayahuasca admixtures and the diversity of cultural practices among different indigenous groups throughout the Amazon. "Broad Spectrum Roles of Harmine in Ayahuasca" addresses the unique biochemistry of ayahuasca vine, namely its harmine content, and how other components of ayahuasca may demonstrate great potential in treating mental disorders. This section ends with "Viva Schultes — A Retrospective (Keynote)," a touching tribute to the late Professor Richard Evans Schultes, PhD, the father of modern ethnobotany. This article highlights his contributions to furthering the knowledge of Amazonian ethnobotany and psychoactive plants and medicines, while protecting the intellectual property and territories of the indigenous communities he loved.

The "Africa, Australia & Southeast Asia" section reveals the dearth of information on psychoactive species from these areas in comparison to the previous section on ayahuasca and the Amazon.

"Kabbo's !Kwaiń: The Past, Present and Possible Future of Kanna" provides a comprehensive history of kanna (*Sceletium tortuosum*, Aizoaceae), a succulent plant from South Africa with potential uses for depression and anxiety. A proprietary kanna extract is now sold globally as Zembrin®

(HG&H Pharmaceuticals; Bryanston, South Africa), which contains the active alkaloids mesembrine, mesembrenone, and mesembrenol as serotonin inhibitors. Traditionally, kanna has been used to enhance mood, to increase sense of wellbeing, for its intoxicating and sedative effects, and as a treatment for insomnia and addiction. Notably, Zembrin is also the first documented case of successful prior informed consent with benefits-sharing between an indigenous group and a pharmaceutical company in the commercialization of a traditional psychoactive medicine.

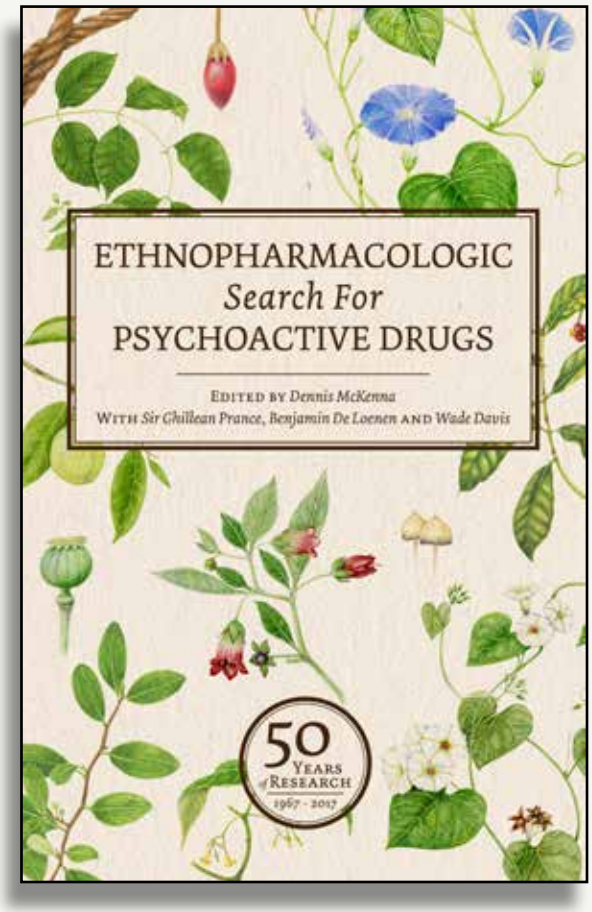
The next chapters address kratom (*Mitragyna speciosa*, Rubiaceae) from Southeast Asia and ibogaine derived from *Tabernanthe iboga* (Apocynaceae) roots from West Central Africa as possible treatments for opioid dependence. "Kratom (*Mitragyna speciosa*) as a Potential Therapy for Opioid Dependence" discusses the controversy surrounding the use of kratom due to the dangers of product contamination, adulteration, or misuse. Kratom is difficult to regulate, as most sales in developed countries currently occur in the online marketplace. The article emphasizes the need for more studies on the phytochemistry and the mechanisms of action. The opioid-like alkaloids (e.g., mitragynine, 7-hydroxymitragynine, corynantheidine) in kratom have the potential to be templates for the creation of new medicines. Human clinical trials could rectify current misinformation about a promising plant that may ameliorate the current opioid addiction crisis.

"The Ibogaine Project: Urban Ethnomedicine for Opioid Use Disorder" shows clinical evidence of ibogaine's efficacy for opioid detoxification. Traditional use of *T. iboga* as a spiritual sacrament offers a compelling twist on healing addiction in modern society.

Following these chapters is "Psychoactive Initiation Plant Medicines: Their Role in the Healing and Learning Process of South African and Upper Amazonian Traditional Healers," a compelling comparison of psychoactive plant rituals essential to shamanic healer initiation in Southern African and Amazonian indigenous traditions. The use of plants as spiritual learning agents here suggests that a neural disruption is necessary for perceptatory change followed by behavioral modifications.

Then, "Psychoactive Australian Acacia Species and their Alkaloids" explores several Australian *Acacia* species (Fabaceae), which are called wattles in Australia, and their psychoactive constituents are compared to ayahuasca. These psychoactive acacias have diverse traditional medicinal uses: cessation of smoking, pain relief, fish poison, alkaline ash sources for tobacco chewing, and as coffee (*Coffea arabica*, Rubiaceae) and tea (*Camellia sinensis*, Theaceae) substitutes. Many discoveries of new alkaloids from the genus *Acacia* in general, as well as those from native Australian species specifically, are covered. Lastly, the chapter mentions how the commercialization of native Australian acacias for bark extracts exploits vulnerable wild populations.

The section's keynote, "From 'There' to 'Here': Psychedelic Natural Products and Their Contributions to Medicinal Chemistry," discusses the promise of psychoactive plants and fungi in the discovery, creation, and modification of novel, therapeutic, and entheogenic compounds, as well as the gained benefits of understanding the mysteries of human consciousness and neurobiology. This psychedelic natural products compilation combines the science and the sacredness of keystone psychoactive substances and species such as psilocybin (derived from various species, including *Psilocybe cubensis*, Hymenogastraceae), peyote (*Lophophora williamsii*, Cactaceae), ergot (*Claviceps purpurea*, Clavicipitaceae), and *ololiuqui* (*Rivea corymbosa*, Convolvulaceae). This portion concludes with a summation of major chemical groupings derived from such species like tryptamines (DMT, 5-MeO-DMT, bufotenine), phenethylamines (mescaline), and ergolines (ergine).



"Mexico & Central America" is the smallest section of all with three articles.

"Fertile Grounds? – Peyote and the Human Reproductive System" focuses on the traditional use of peyote for women's reproductive issues including childbirth and afterbirth. Traditional uses of peyote in babies and children have been documented and are considered safe. Furthermore, there is a cultural belief that peyote consumption throughout all stages of pregnancy and childbirth aids individuals in attaining healing abilities to eventually become a healer for the people.

"Mescal, Peyote and the Red Bean: A Peculiar Conceptual Collision in Early Modern Ethnobotany" detangles the misidentifications and misconceptions of three formerly confused psychoactive species: maguey (*Agave* spp., Asparagaceae), peyote, and Texas mountain laurel (*Dermatophyllum secundiflorum*, Fabaceae).

"Reflections on the Peyote Road with the Native American Church — Visions & Cosmology" is written by an esteemed attorney who has long represented the Native American Church (NAC), Jerry Patchen. Patchen presents a historical overview of peyote use as a religious sacrament by the NAC, which represents many Native American nations, and the long struggle to legalize peyote for religious use. As a non-Native American, he describes his personal experiences with peyote cultural rites as some of the most transformative experiences of his life within this community. The NAC continues to successfully fight for the religious freedom to partake in the ingestion of the holy sacrament peyote.

The final section pertains to the "Biosphere," which is decidedly broad in scope and composed of articles that did not fit into the other categories.

"Phylogenetic Analysis of Traditional Medicinal Plants: Discovering New Drug Sources from Patterns of Cultural Convergence" describes the field of phylogenetic ethnopharmacology, in which cultural data is merged with analyses of psychoactive plant families in order to predict bioactivities with potential medicinal benefits.

"Ethnopharmacology Meets the Receptorome: Bioprospecting for Psychotherapeutic Medicines in the Amazon Rainforest" reports on Amazonian psychoactive species with potential to treat pressing neurological disorders such as schizophrenia, Alzheimer's disease, and dementia. Approximately 40% of studied species and their compounds have been shown to exhibit CNS activity in vitro.

"A Preliminary Report on Two Novel Psychoactive Medicines from Northern Mozambique" reports on *Aeschynomene cristata* (Fabaceae). This is the only known member of this genus that has been reported to possess psychoactive effects, and laboratory studies are pending.

The volume concludes with "Ethnopharmacology: From Mexican Hallucinogen to a Global Transdisciplinary Science," which attributes Mexican indigenous traditions as early contributors to the social explorations and scientific study of psychoactive drugs and to the field of ethnopharmacology as a whole. The authors suggest *Salvia divinorum* (Lamiaceae) was the first psychoactive plant that sparked widespread public interest in the topic.

While the fields of ethnopharmacology and ethnobotany have evolved, the original inspiration comes from psychoactive plants and fungi, and this relationship remains valuable throughout time. HG

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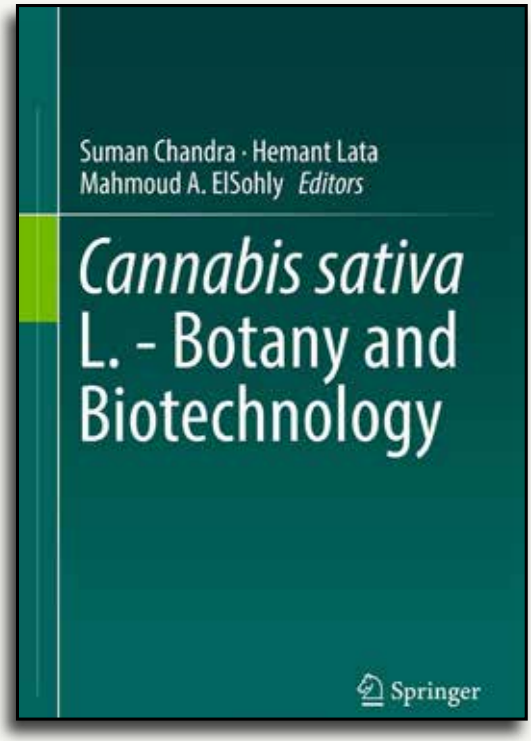
Cannabis sativa L. - Botany and Biotechnology by Suman Chandra, Hemant Lata, and Mahmoud A. ElSohly, eds. New York, NY: Springer International Publishing; 2017. Hardcover, 479 pages. ISBN: 978-3-319-54563-9. $219.99.



What does it take to make a difference in the cannabis (*Cannabis sativa*, Cannabaceae) research field or industry? With research roadblocks that can take years to navigate, the industry's only protection from the Drug Enforcement Administration is an annually reviewed Commerce, Justice, Science, and Related Agencies (CJS) amendment, a lack of consistent regulations, and a ton of myth-information about products and their consistency, efficacy, legality, and safety. Given the state of things in the cannabis domain, the question can be too paralyzing to ask. The cloudiness of the lens and lack of resources to accelerate solutions are essential components of what the authors of this text explore.

Over the last 15 years, cannabis (hemp or marijuana) cultivation has become a major part of the agricultural industry in many countries. Unfortunately, detailed knowledge of cannabis botany and biotechnology seems to be beyond the field experience of many growers, and medical cannabis products continue to be sold without details regarding contents, or even different varieties, extracts, and mixtures sold under the same commercial name. As the famed, pioneering Israeli cannabis researcher Raphael Mechoulam, PhD, explains in the book: "It is unbelievable that neither government agencies nor private foundations have gone ahead or encouraged clinical trials — but this is a fact!"

The book includes quite the cast of characters, from well-established authors to innovative rising stars from academia and the industry. Few other cannabis science books boast such a broad range of disciplines in one binding. For example, the book is edited and co-authored by one of the most-published natural products researchers (Mahmoud ElSohly, PhD), and another author is the director of a lab that specializes in genetic testing for the cannabis industry (Kevin J. McKernan, PhD). Due to the widely dispersed nature of the literature on the topics presented, this blend of experts and perspectives is a potent tonic.

At the beginning, this text seems like any other academic book, but the innovative interests of the authors become clearer as the reader proceeds through the sections on ancient history to state-of-the-art research applications. I immediately began implementing it as a source in my own research proposals and business strategies. Biotechnology plays an important role in propagation, conservation of varieties, and improvement in medicinal plants. Chapters 13-21 focus on this role, and an entire chapter is devoted to comparing state-of-the-art methods for cannabis micropropagation.

The book covers a vast range of cannabis science topics. Authors explore the existing knowledge and identify numerous areas for further research, including botany and horticulture, pharmacology and methods of analysis, chemical and morphological phenotypes in breeding, morpho-anatomy of cannabis, biosynthesis and biotechnological applications, allergenicity to cannabis and methods to assess personal exposure, genomics and molecular markers, micropropagation, hairy root culture as a biotechnological tool, cannabis endophytes and their applications in breeding and reproductive fitness, and contaminants of concern in cannabis.

Aside from the botanical and biotechnological aspects of the plant, the book ends with a chapter on product safety and contaminants. While academia and industry seem to be hitting their stride with the plant, there have been serious issues due to sloppy, unethical, and dubious operators in the cannabis space. The book describes a number of surprising lessons the global cannabis industry hopefully has learned. While the plant is relatively innocuous and non-toxic, humans find an endless combination of ways to make it less safe, as with many mass-produced commodities. This includes spraying cannabis plants with fertilizer made from human feces (in Europe) or untreated manure (in North America), and a company that was caught repacking a product that was targeted at cannabis growers and contained an illegal pesticide. These behaviors can lead to costly fines and recalls and adversely influence policy and regulatory decisions.

The book also discusses aspects of cultivation that enhance or inhibit different characteristics and qualities of the plant, including its genetics, nutrients, and microbiome. A plant grown for cannabidiol (CBD) should not be grown for fiber for many reasons. Hemp, a name that refers to plants in 22 genera, is used to make textiles like rope, clothing, and industrial products; *Cannabis* produces a hemp variety. Hemp varieties may be more susceptible to heavy metal accumulation and contamination because of the increased fiber content and lower standards for the cultivation of products that are not grown for human consumption.

The compiled information on hemp is useful for those who work across disciplines, in research, regulations, and industry. This is important because hemp plants are grown differently from medicinal plants, mostly to improve fiber production over resin production. The tools and resources exist to improve cannabis agriculture, but we need academia and industry to work together more closely to use the knowledge base and truly create a resurgence of cannabis' place in the global economy.

This book succeeds because it combines basic sciences such as botany with applied sciences such as biotechnology. This combination has proven powerful enough to solve many issues, such as how to decontaminate dried flower tops or apply genetic testing to breed specific medicinal chemovars (chemical varieties). The book also identifies a number of research projects that could allow cannabis (as hemp or a medicinal plant) to have a significant economic resurgence. It is also useful for students who are looking for long-term projects or industry entrepreneurs who are trying to earn licenses or increase funding opportunities by using innovative research technology. Personally, the book has been a useful guide for my partners in the cannabis industry to help choose and focus on projects for various cultivation operations.

I recommend this book to many people, especially cannabis growers, in hopes that it encourages cultivation operations to work with agricultural specialists, biochemists, and analytical chemists to enable a consistent and global supply of standardized medical cannabis for patients and researchers. This book will be of considerable importance not only in summarizing present-day knowledge but also in advancing innovations in the cultivation and use of cannabis. HG

—Jahan Marcu, PhD
COO and Director of Experimental Pharmacology and Behavioral Research
International Research Center on Cannabis and Mental Health
New York, New York

Barbara 'BJ' Johnston 1932-2018

Barbara Johnston, the first managing editor of *HerbalGram*, died on September 28, 2018, at the age of 86. She lived a full life that started in the small village of Onekama in northern Michigan. Shortly after moving to Austin, Texas, in 1983, she was hired to serve as the editor of the second issue of what was then Mark Blumenthal and Rob McCaleb's newly founded newsletter *HerbalGram*. Johnston continued to edit *HerbalGram* after the foundation of the American Botanical Council (ABC) in 1988 until her retirement in 2000.

Johnston's childhood in Onekama was one of resourcefulness and hard work. Educated in a one-room schoolhouse, she made up for a lack of academic rigor by reading and learning independently of the classroom and, through a love and talent for music, earned a partial scholarship to study voice and piano performance at Michigan State University. After college, she married Jerry Johnston, and the couple lived in Chicago, Illinois, through the birth of their first two children. When her husband was offered a job at Boeing in Seattle, Washington, they packed up their small family and moved across the country.

Johnston's son Michael, who was nine months old at the time, is well-acquainted with this part of his family's history. "Barbara told the story many times of driving over the Rocky Mountains, at night, with the kids screaming in the back of the car," he wrote (email to M. Blumenthal, January 25, 2019). The Johnstons stayed in Washington State for decades, and Barbara and Jerry had two more children.

Once her children were in school full-time, Johnston began to work outside the home and tried out a number of jobs before being hired as a sales associate at a fabric store. Johnston, who loved to knit and sew, suggested that the store stock yarn and offered to teach sewing and knitting classes. The idea was a success, and Johnston found her niche as a teacher and crafter. Around this time, she also began selling her own needlepoint designs and worked with the National Needlework Association to organize trade shows throughout the United States.

The Johnstons divorced and she moved to the city of Los Gatos, California, where she made frequent trips to Los Angeles to host the needle arts program "Needlecraft" on KOCE-TV, a public broadcasting network. In 1981, she received a Los Angeles-area Emmy Award for her work on the educational television show. After her brief sojourn in California, she moved to Austin and became involved in the fledgling newsletter that would become the basis for the founding of ABC.

In Johnston's busy crafts room, she helped create and edit the first issues of *HerbalGram,* which was an eight- then 12-page newsletter. It then grew to 16, then to 24 pages. For the earliest issues, she laid them out using what is now the old-fashioned cut-and-paste method, where articles, the *HerbalGram* masthead, and clip-art were literally cut and pasted onto a layout board and then photographed onto a metal plate by the printer.

"BJ literally had her hands all over every issue," said Blumenthal.

He continued: "She was an amazingly intelligent, energetic, creative, and productive person. I don't believe I've ever known anyone who was so well read — she was truly a voracious reader. She started her own magazine, *Doll Makers Journal*, and became a nationally known expert in her field."

Cecelia Thompson, ABC's finance coordinator, who has worked at the organization since 1988, said: "I will always remember Barbara for her incredible creativity, passion for life, fun-loving nature, and, especially, her quick wit. She brought sunshine to a lot of people's lives in work and play. Of course, with her love of margaritas, we enjoyed many happy hours together! At ABC, she made sure that *HerbalGram* had a '3R' rating: respected, revered, and read."

In preparation for the 50th anniversary of the 1939 film *Gone with the Wind*, the Texas Memorial Museum at the University of Texas at Austin hired Johnston to do detailed, expert work to restore the degraded lace on one of the iconic costumes worn by actress Vivien Leigh, who played Scarlett O'Hara.

"She was that good, and she was that nationally respected for her mastery of needlework arts," Blumenthal recalled.

Johnston never stopped learning and was a frequent visitor to the Austin Public Library. Her love of crafting became a philanthropic hobby and she knitted throw blankets and socks to donate to friends, charities, and wounded veterans. Her home became a destination for her many friends from all walks of life to meet, work on their latest projects, and socialize.

"Barbara's years in Austin were, by her own admission, her best," wrote Michael Johnston. "She did what she wanted, when she wanted, how she wanted… She even started to say 'y'all.'"

Barbara Johnston is survived by her brother Ted Guimond and children Linda, Michael, Scott, and Ara. She was predeceased by her brother William Guimond and her parents, Anice and William. A celebration of her life was held on January 26, 2019, at ABC's headquarters in Austin. HG

—Hannah Bauman

Peter John Semper, Jr. 1931-2018

Peter Semper, who was one of the founding forces for the Council for Responsible Nutrition (CRN) and its first executive director, died on December 13, 2018. In addition to his work at CRN, Semper worked tirelessly to expand consumer access to herbal and dietary supplements through lobbyist efforts and his supplement-centric public relations agency.

Semper was born on February 10, 1931, in Lindsay, California. As the Great Depression gripped the United States, his family moved frequently and Semper began working at an early age: first in the fields and orchards, then as a paperboy when his parents settled in San Francisco, California. He graduated high school at the age of 15 and held a series of jobs until he enlisted in the US Air Force in 1950. His duties included training in jet electronics and as an instructor for flight simulators. When his four-year commitment in the armed forces ended, Semper attended Los Angeles City College and earned a degree in marketing and communications. With this degree, he worked for a few years as an account executive at an advertising agency in Los Angeles. According to longtime friend Mark Blumenthal, one of Semper's early clients was Altec Lansing, a manufacturer of large loudspeakers for movie theaters, which stimulated his interest in publicity and public relations (email, February 2, 2019). Semper eventually opened his own agency, Semper Moser, in 1968.

A year later, in 1969, Semper gained Bill Thompson of the William T. Thompson Company (then one of the largest supplement companies in the United States) as a client. James Turner, an attorney at the Swankin & Turner office in Washington, DC, and CRN's general counsel from 1973 to 1975, recalled that "Thompson pulled Peter, his old Marina del Rey [California] friend who lived on a sailboat, onto his company team with the assignment to get dietary supplements off the fringe and into the mainstream" (email to M. Blumenthal, January 1, 2019).

This business partnership ignited Semper's interest in the subject of nutrition and supplementation, and he gradually shifted his entire business to specialize in the nascent-but-growing dietary supplement industry. Semper further immersed himself in the business of dietary supplements when, in 1973, the US Food and Drug Administration (FDA) proposed stringent legislation regarding the manufacture and sale of vitamins and minerals. The proposed legislation required review and approval by the FDA's over-the-counter expert health advisory committee for any product that provided more than 150% of the FDA's recommended daily allowance of a vitamin or mineral. The industry perceived this action as the government's attempt to regulate supplements as drugs based on nutrient levels (referred to as "potency") alone. The outcry by the industry spurred Semper to register as a lobbyist and protest the FDA's proposal.

This action by the FDA also inspired the founding of CRN, a trade association that would represent the interests and concerns of dietary supplement and functional food manufacturers.

John "JB" Cordaro, former president and CEO of CRN (1982-2002), relied on Semper's advice and guidance as CRN expanded. "I learned quickly in the early days of my tenure as CRN president and CEO that Peter Semper was my North Star," wrote Cordaro (email to M. Blumenthal, January 3, 2019). "With Peter's encouragement and support, I set out to establish a CRN Code of Ethics for our members with real enforcement teeth and Guidelines for Safety and Quality Standards. These achievements would stand us in good stead with regulators, our existing and prospective members, and even among some of our critics…. In addition, Peter exemplified the selfless characteristic [with] a willingness to get things done and not needing to be known for what he achieved."

Thanks in part to Semper and CRN's leadership, Congress passed the 1976 Proxmire Amendment, which prohibited FDA from establishing standards to limit the potency of vitamins and minerals in food supplements. Around this time, Semper and Thompson supported other industry projects, including *Natural Foods Merchandiser*, Natural Food Expo (now the Natural Products Expo), and the Natural Foods Network, a gathering of natural products brands that became a key basis of the national expansion of the Austin, Texas-based Whole Foods Market.

Turner worked closely with Semper through the founding of CRN and the turbulent years of the early dietary supplement market in the United States. "Semper's shrewd, clever, strategic thinking saw the power of combining consumer and producer interests," he wrote. "Peter made towering contributions to the foundations of the natural food, dietary supplement, and integrative health markets as we know them today.... He expanded my life, and enhanced the health of millions of dietary supplement consumers."

In the midst of his work with CRN, Semper continued to run his supplement-oriented advertising and public relations agency. He also served on the board of directors of the National Nutritional Foods Association (now the Natural Products Association) in the late 1980s, as well as various other advisory boards, and served as an informal consultant to many companies.

In his personal life, Semper was an avid surfer and outdoorsman. He also maintained a deep interest in the history of California and Mexico, organic gardening, and citrus cultivation, managing groves in Florida from the 1990s until his death. "Peter wanted to be remembered for the laughter and joy he brought others, even strangers, and for the delight he brought others through his gift for storytelling," wrote Teri Semper, Semper's wife (email to M. Blumenthal, January 23, 2019). "He was most proud of his work in the dietary supplement industry. He was interested in his personal freedom and the collective freedoms of his fellow Americans. His was a well-lived life."

Peter Semper is survived by his wife Teri, brother George, sons Peter and Chris, and his grandchildren, nieces, and nephews. He was predeceased by his daughter Jacki. HG

—Hannah Bauman

Rudolf Hänsel 1920-2018

Editor's note: *A previous version of this obituary appeared in the June 2018 edition of* Planta Medica*, the journal of the Society for Medicinal Plant and Natural Product Research (GA). Additional information on Hänsel's accomplishments has been added by* HerbalGram *editorial staff.*

Rudolf Hänsel, Dr. rer. nat., Professor Emeritus of Pharmacognosy (1956-1987) at the Free University of Berlin, died on June 14, 2018. He was born in Zinnwald, Bohemia (now part of the Czech Republic), in 1920 and studied pharmacy at Ludwig Maximilian University of Munich. After having obtained a license to work as pharmacist in 1947, he completed his doctoral dissertation in 1950, followed by his habilitation* in 1955, also at Ludwig Maximilian University. In 1956, he was appointed as professor of pharmacognosy at the Institute of Pharmacognosy at the Free University. Until his retirement in 1987, he was director of the institute and a very successful university teacher and researcher who was well-known in Europe. The GA granted him an honorary membership in 2003.

Hänsel's scientific work was characterized by natural product research in the field of European and other medicinal plants (e.g., kava [*Piper methysticum*, Piperaceae]). His extensive scientific work started with chemical isolation, structural characterization, and biological testing and continued to elaborate analytical procedures that were published in monographs of pharmacopeias. German-speaking students of pharmacy likely know the famous textbook, originally titled *Lehrbuch der Allgemeinen Pharmakognosie* (*Textbook of General Pharmacognosy*), which he co-authored with Ernst Steinegger in 1963. Hänsel oversaw nine editions of this textbook until 2010, when he worked together with Otto Sticher, also an honorary GA member. It was rather spectacular that an author was able to edit a textbook with excellent quality and updated content over such a long time period. Hänsel and Sticher also are mentioned in the current 10th edition from 2015. Readers of *Hagers Handbuch der Pharmazeutischen Praxis* (*Hager's Handbook for Pharmaceutical Practice*) know the name Rudolf Hänsel because of his long editorial stewardship of this lexical reference work. He was also the co-author of the textbook *Rational Phytotherapy: A Physician's Guide to Herbal Medicine*, with his colleague professor Volker Schulz, the fourth edition of which was translated into English and revised by Varro E. Tyler, PhD. After Tyler's death, the fifth edition was revised by Mark Blumenthal.

Stefan Gafner, PhD, chief science officer of the American Botanical Council, commented: "During my undergraduate years, Professor Hänsel was known to every pharmacy student since his *Lehrbuch der Pharmakognosie und Phytopharmazie* [*Textbook of Pharmacognosy and Phytopharmacy*] — which was the title of the fourth edition of this textbook (although among students it was better known as the *Steinegger-Hänsel* in reference to the two authors' names) — was the basis of our education in phytochemistry. It has always been among my favorite textbooks on pharmacognosy, and one that I hope will eventually be translated into other languages to make its content available beyond the German-speaking population."

After Hänsel's 80th birthday, he was honored with the Aulus Cornelius Celsus Medal by the German Central Association of Physicians for Natural Remedies in 2001 and the honorary membership of the German Pharmaceutical Society/National Group Bavaria.

Due to his scientific work and his textbooks, Hänsel will always be remembered by researchers active in natural products chemistry and pharmacognosy. HG

—Prof. Dr. Matthias F. Melzig
Freie Universität Berlin
Berlin, Germany

* Habilitation consists of the completion of an independent research project that qualifies the investigator to teach at a university; it is a prerequisite in certain European countries to become a professor.

Gary Raskin
1943-2018

Gary Raskin, co-founder and co-owner of The Ginseng Company in Reseda, California, died on September 4, 2018, a few weeks shy of his 75th birthday. He was born in Chicago, Illinois, on September 26, 1943, and was the oldest of four children. At the age of 10, his family moved to Los Angeles, California.

Raskin earned a bachelor's degree from Sonoma State University, then worked as a psychiatric technician at Sonoma State Hospital before moving back to West Los Angeles and landing a similar position at UCLA's Neuropsychiatric Institute. He met and married Linda Collings in the early 1970s and adopted her daughter, Dyan.

To support his young family, Raskin worked a second job and became fatigued from a burdensome schedule. A friend suggested that he take ginseng (*Panax* spp., Araliaceae) as a way to boost stamina, which he did with good results. This experience inspired him to learn more about ginseng, and, out of the back of his truck, he began to sell ginseng roots to health food stores. A business was born in 1973 and, in January 1974, The Ginseng Company was officially formed and incorporated. This year also marked the birth of Raskin's second daughter, Angela.

With his characteristic easy manner, tireless effort, and honest work ethic, Raskin's business grew. He gradually added other products until The Ginseng Company matured to become a distributor of mostly herbal and dietary supplements and body care products. His wife, Linda, retired from her position with the US Postal Service and ran the warehouse, occasionally making sales visits to health food stores to help grow the company's wholesale distribution.

In 1993, Raskin and his longtime sales representative Rick Seibert developed their own line of ginseng products under the brand name Imperial Elixir. GINCO International was incorporated in May 1994, and the product line took off.

The Raskins made a difficult business decision to close The Ginseng Company in June 2005, making their retirement the following year a little easier.

"I remember Gary as a thoughtful and serious guy, who didn't let the idea of making a buck take precedence over what he thought was right," wrote Howard Mechanic, a friend and business associate, who, during the 1970s and 1980s, owned a similar small wholesale business called Pure Planet Products in Arizona (email to M. Blumenthal, November 17, 2018). "He wanted to create a business that would allow him to make a living while doing good."

Mark Blumenthal, founder and executive director of the American Botanical Council, said: "Gary was a true pioneer in the ginseng and herb industry. Back in the days when I owned Sweethardt Herbs Inc., my company that wholesaled many ginseng and other herbal products that Gary also sold, we were friendly competitors and suppliers to each other. Gary was always easy and fun to deal with, always followed through on his promises, and paid his bills on time. He was an honest and honorable man."

Herb industry leader Michael McGuffin, president of the American Herbal Products Association, reminisced about his early days in the herb industry and his relationship with Gary (email to M. Blumenthal, December 24, 2018):

> When Janet Zand and I started our herb company in 1980, Gary gave us our first break when he agreed to have The Ginseng Company distribute our brand to stores in the southern California area. And then he gave us our second and third breaks when he introduced us to Auro Trading Ltd. and Feather River Company, which became our next distributors, covering stores in northern California.
>
> After I dropped off an order at The Ginseng Company, Gary and I often found a few minutes to sit together in his office and talk about our businesses in the herb industry that was developing around us at the time. I will always remember Gary as a gentle and generous man, and for his ever-present supply of ginseng that he shared with me during [those] times.

This author is eternally grateful for the opportunity Gary Raskin gave me to join his company and the natural products industry in 1977. I admired his integrity and honesty as a business owner, the courageous yet careful entrepreneur he was, his wry sense of humor, his respect for others, and dedication to his family and business. He will be greatly missed by the employees at GINCO International and by many friends and colleagues he made in more than 30 years of supplying ginseng and other herbal products in the southern California area and nationwide.

Gary's passions in life were his family, business, sailing, biking, conga drumming, and sushi.

He is survived by his daughters Dyan Collings Ralph and Angela Raskin. HG

—Rick Seibert
Vice President of Sales and Marketing
GINCO International
Simi Valley, California

Brian Keating
1956-2018

Herb and tea (*Camellia sinensis*, Theaceae) industry veteran Brian Keating died unexpectedly on September 2, 2018, of a heart attack. Keating founded Sage Group, a Seattle, Washington-based natural products consulting group, to assist clients with creative, strategic, and technical support. Businesses, brands, and events, such as Whole Foods Market, Tazo Tea Company, World Tea Expo, and many more, have all benefitted from Keating's knowledge of the tea market in the United States and passion for high-quality, artisanal tea products.

Keating was born in Denver, Colorado, on May 25, 1956. Though he never finished high school, he enjoyed reading and learning in his own way. He entered the world of natural products as an herb and spice buyer for a natural foods store in Denver, and he further dabbled in the culinary world by becoming a chef and spice buyer at a Moroccan restaurant.

In the mid-1970s, the tea market in the United States was small. However, Keating had a passion for tea and believed that the US market had untapped potential. He formulated his first product, a tea-based energy drink called SPORTea, in 1982 through his company Ultimate Performance Products, Inc. In 1996, Keating assumed ownership of a Seattle specialty tea shop called The TeaCup, where he sold a large selection of bulk teas, tea products, and drinks he formulated himself.

As general knowledge and availability of fine teas grew, Keating saw an opportunity for further expansion and founded Sage Group to aid the fledgling market. Sage Group's clients have included companies such as Valensa, Nutraceutix, New Chapter, Amway, Starbucks, and many others in the United States and internationally. Keating expanded the scope of his consultancy to include other herbs, spices, nutrients, and flavorings, but tea remained his passion and focus, and he believed that tea could grow to rival coffee (*Coffea arabica*, Rubiaceae) in popularity in the United States.

Aromatherapist Mindy Green, RH (AHG), recalled that it was Keating's nature to explore every avenue and try different things. "Brian was the quintessential Gemini, flashing between a wide variety of social circles and diverse business clients," she wrote (email to M. Blumenthal, January 2, 2019). "He was a superior networker, wicked smart, uniquely quick witted, funny as hell, creative and talented, as well as being genuine, warm, empathetic, honest, and kind…. As my business partner, mentor, and coach, Brian is irreplaceable. As my friend, he will be sadly missed every day."

In 1993, Sage Group published its first "US Tea is 'Hot' Report" that offered trend analyses, market insights, and other resources for those in the tea business. The report was well-received by the industry, and it was then that Keating closed his tea shop in order to expand the offerings of Sage Group. The group would publish seven editions of the report and added a kombucha market report in 2008 and a matcha report in 2013. Keating also co-authored the American Botanical Council's first tea market report for *HerbalGram* issue 105.[1]

Keating recognized a unique opportunity in 2003: the first World Tea Expo. He was the lead speaker for the inaugural event, a role he reprised nearly every year after that. His networking skills helped attract the participation of large conglomerates such as Nestle, Unilever, and Pepsi, and other consumer product manufacturers. The World Tea Expo, which is now run by Informa, is held annually in June in Las Vegas, Nevada. The event currently features an exhibit hall with hundreds of exhibitors, a new products showcase, tasting events, educational sessions, an awards ceremony that recognizes lifetime achievements in the tea business, and expert speakers from around the world.

Keating further guided the expansion of the US tea market through his work with Whole Foods Market in 2006, when he became the company's first tea buyer and blendmaster for its subsidiary Allegro Coffee Company. In this position, he helped establish Whole Foods' in-house line of tea beverages and developed 40 new products for that line.

Rob McCaleb, president of the Herb Research Foundation and former research director for Celestial Seasonings, worked with Keating and Sage Group during his tenure at Celestial Seasonings, and their professional relationship grew into a personal friendship. McCaleb fondly remembered Keating's dynamic personality, love of music, and caring nature. "For many years, he [was] such a close friend to me, and to so many others," McCaleb wrote (email to M. Blumenthal, January 5, 2019). "He was simply a giant in the tea world. I don't know of anyone who had Brian's depth of knowledge about tea, about the business of tea, the growing and production of tea, the science of tea, the WORLD of tea."

Brian Keating is survived by his sister, Pam Herbst, and niece, Lindsay Herbst. Remembrances of his life were held in Seattle and Boulder, Colorado, in September and October 2018, respectively. HG

— Hannah Bauman

Reference

1. Keating B, Lindstrom A, Lynch ME, Blumenthal M. Sales of tea & herbal tea increase 3.6% in the United States in 2014. *HerbalGram*. 2015;105:59-67. Available at: http://cms.herbalgram.org/herbalgram/issue105/hg105-teamktrpt.html. Accessed January 16, 2019.

Publications

American Herb Association Quarterly Newsletter: $20/yr. AHA, P.O. Box 1673, Nevada City, CA 96969.

Australian Journal of Herbal Medicine: Quarterly publication of the National Herbalists Association of Australia (founded in 1920). Deals with all aspects of Medical Herbalism, including latest medicinal plant research findings. Regular features include Australian medicinal plants, conferences, conference reports, book reviews, rare books, case studies, and medicinal plant reviews. AUD/$96 plus AUD/$15 if required by airmail. National Herbalists Association of Australia, P.O. Box 696, Ashfield, NSW 1800, Australia.

Medical Herbalism: Subtitled "A Clinical Newsletter for the Herbal Practitioner." Edited by Paul Bergner. $36/yr, $60/2 yrs. Canada $39/yr. Overseas $45/yr. Sample/$6. Medical Herbalism, P.O. Box 20512, Boulder, CO 81308.

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Red Clover (*Trifolium pratense*, Fabaceae)

Red clover is a perennial herb that is used primarily as fodder for livestock.[1] Clover also has been used in agriculture as a nitrogen-fixer, as it increases soil fertility through the production of nitrogenous compounds in its root system. In Western and Chinese traditional medicine practices, clover is used both internally for conditions such as congestion and lymphatic system disorders and externally for skin disorders like psoriasis and eczema. The primary modern research interest in red clover is for its isoflavone content.[2] Isoflavones are a type of phytoestrogen that may have a potential benefit for those going through menopause and experiencing symptoms such as hot flashes and bone density loss. Red clover is also the state flower of Vermont[3] and the national flower of Denmark.[4]

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