Grape Seed Profile • Kratom Crackdown • 2017 Herb Market Report
Hawthorn for Heart Failure • Cannabis Research Review

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GOLDENSEAL'S Conservation Status

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letters to the editor

Dear Editor,

I write to congratulate you on [Connor Yearsley's] article "The Botanical Endeavour of Sir Joseph Banks: Historic Prints from His Florilegium Now Available Like Never Before."

I share your interest in and admiration for Sir Joseph Banks. In fact, I own one of the special edition prints [of *Leucas decemdentata*, Lamiaceae]. How this came to be is told in Paul Cox's book *Nafanua*.

During my tenure at Nature's Way, I worked with Ken Murdock and Professor Paul Cox to raise money to purchase the Falealupo rainforest in Samoa. I am one of the friends who purchased a Banks print in support of this project. Incidentally, we did raise the money, and the rainforest was saved.

This special edition print is in my office and has been an "old friend" for many years. [Connor's] article is a wonderful contribution to preserving the history and remarkable story of the Florilegium. I thought it might interest you to know that among [ABC's] circle of friends there are a few that have a small part in that history.

With much appreciation,

Loren Israelsen
President, United Natural Products Alliance
Salt Lake City, Utah



Cover of *HerbalGram* issue 118

Dear Editor,

Two copies of your handsome *HerbalGram* journal have just arrived, complete with Connor Yearsley's excellent and beautifully illustrated article about Banks' Florilegium.

It's always a pleasure to read a well-researched and accurate account of a subject one knows well, and he has hit the mark on every occasion — and added quite a few bits of knowledge to boot. Many congratulations.

I do hope that the article will receive the recognition it deserves in the United States. Thanks to his generous comments, I hope too that it will generate renewed interest in the original engravings in the States. The book has produced a stream of interest (and sales) for the single prints we still have available, especially from Australia and New Zealand.

With all good wishes,

Joe Studholme
Chairman, Editions Alecto
(Publisher of Joseph Banks' Florilegium)
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dear *reader*

As I write this column in the record July heat here in Texas, I recall this time in 1983 when we published the first issue of *HerbalGram*, then titled "Herb News" with "Herbalgram" as a subtitle. Over the past 35 years, that eight-page newsletter has evolved into the peer-reviewed journal/magazine that you are reading now. On page 16 of this issue, we present a brief history of this publication, which, after its first five years, became the basis for ABC's founding. Even though ABC produces other serial publications (e.g., the monthly HerbalEGram, twice-monthly HerbClips, weekly Herbal News & Events, and quarterly Botanical Adulterants Monitor), *HerbalGram* remains ABC's flagship publication, and, to many people in the medicinal plant community in the United States and internationally, the publication for which ABC is best known.

This issue's cover story reflects ABC's ongoing interest in and advocacy for the sustainability of medicinal, aromatic, and other beneficial plants. We present an in-depth exploration of the conservation status of goldenseal, a popular native North American medicinal plant, the root of which has been used for a variety of medicinal purposes by Native Americans, European settlers, Eclectic physicians, and the modern herbal community in the United States and beyond.

This is the second time that one of Steven Foster's compelling photographs of goldenseal has graced the cover of *HerbalGram.* Issue 41, published in the fall of 1997, featured a cover story by Joy Bannerman on goldenseal's inclusion earlier that year in Appendix II ("species that are not necessarily now threatened with extinction but that may become so unless trade is closely controlled") of the Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES), an international treaty that currently has 183 signatories (or Parties). In her article, Bannerman identified the need for reliable population biology studies of goldenseal in its native habitat in eastern North America. In this issue, botanists and conservation experts Leah Oliver and Danna Leaman, PhD, present an extensive review of the current status of wild goldenseal populations. Over the past 20-plus years, increased availability of cultivated goldenseal root and rhizome has helped reduce the demand for wild-harvested material. However, the relatively long time it takes for goldenseal roots and rhizomes to grow adds to the value of the material and its scarcity as a wild crop. Other threats also remain.

Sales of herbal dietary supplements in the United States increased 8.5% in 2017, reflecting consumers' continued interest in and commitment to natural remedies. As described in our annual Herb Market Report, total retail sales of herbal supplements exceeded $8 billion for the first time last year. *HerbalGram* Managing Editor Tyler Smith and co-authors have compiled and interpreted retail sales data provided by the market research firms SPINS and IRI, and *Nutrition Business Journal*. Our tip of the *HerbalGram* hat to co-authors Kim Kawa, Veronica Eckl, Claire Morton, and Ryan Stredney for their collaboration on this report, which is often one of the most-cited articles we publish.

As part of our occasional series of articles on "herbal legacy companies" (companies that are 100 years old or older), we present Karen Raterman's story on Thayers Natural Remedies, which was founded in 1847 by Henry Thayer, MD. The company still produces a variety of herbal products with ingredients used in its original formulations, including slippery elm lozenges. Slippery elm is one of the few botanical ingredients that is approved as a safe and effective nonprescription (i.e., over-the-counter) drug ingredient by the US Food and Drug Administration (FDA). The mucilage in slippery elm bark has a soothing effect on inflamed mucous membranes and is approved for symptomatic relief of sore throat.

There's been more activity in the kratom domain. *HerbalGram* Assistant Editor Connor Yearsley provides an update on some of the developments on kratom since his extensive cover article on this Southeast Asian tree was published in *HerbalGram* issue 112 in 2016. According to his update, the FDA has pointed to limited, inconclusive data to intensify its warnings about leaf preparations of the plant and also disregarded relevant scientific studies that demonstrate important differences between the kratom alkaloids and common opioids. While we are concerned about reports that some kratom products have been determined to be contaminated with a type of *Salmonella*, we hope that regulatory agencies will consult and interpret the most recent scientific and clinical findings in a rational manner for the best interests of the general public.



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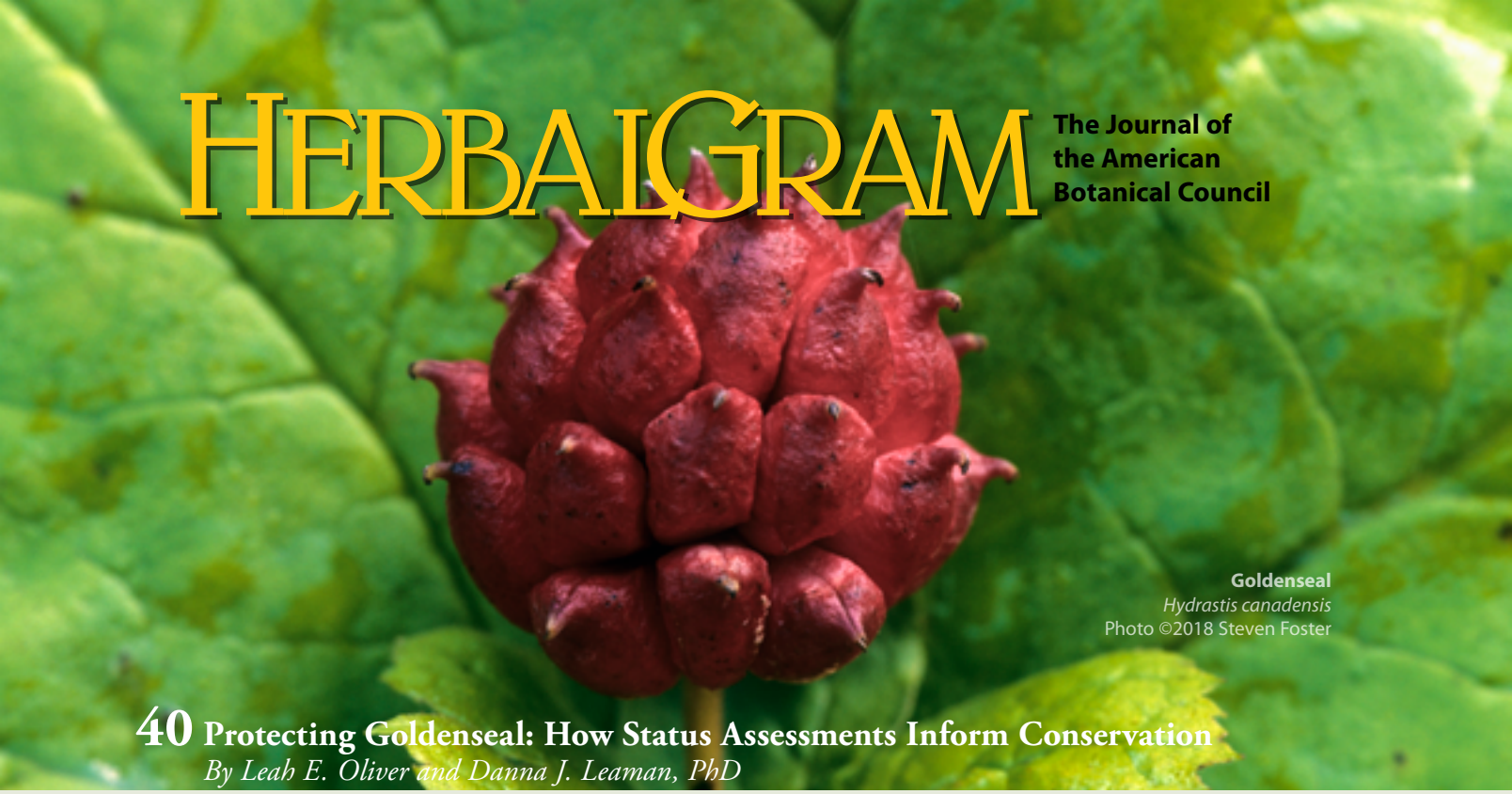
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Goldenseal
Hydrastis canadensis
Photo ©2018 Steven Foster

40 Protecting Goldenseal: How Status Assessments Inform Conservation
By Leah E. Oliver and Danna J. Leaman, PhD

Recently, the International Union for Conservation of Nature (IUCN) published the first global Red List assessment for goldenseal (*Hydrastis canadensis*, Ranunculaceae), which categorized this North American perennial as Vulnerable, meaning it is "considered to be facing a high risk of extinction in the wild." This assessment built on a previous global ranking update by the nonprofit NatureServe. These complementary conservation assessments are intended to inform policy, legislation, and conservation actions to prevent extinction and improve conservation status. While increased commercial cultivation of goldenseal in recent years has helped alleviate pressure on wild populations, the species still is threatened by land conversion, overharvesting, low genetic diversity, a scattered distribution, and other factors. For this species, the authors emphasize the need for field inventories, improved protection, sustainable production, preservation of different genotypes, and other strategies. This article also takes a broader look at the significance of IUCN and NatureServe assessments and compares the methodologies of each system.

56 Kratom Crackdown: FDA Intensifies Warnings with Limited, Inconclusive Data
By Connor Yearsley

The US Food and Drug Administration (FDA) recently continued its crackdown against leaf preparations of the Southeast Asian tree kratom (*Mitragyna speciosa*, Rubiaceae). To support its position, the FDA cited limited, inconclusive death data. In addition, the FDA used a computer model to conclude that kratom is "an opioid" but apparently failed to consider scientific studies that show important distinctions between the kratom alkaloids and other, more common opioids. The US Drug Enforcement Administration (DEA) has indicated it soon could decide whether to place kratom alkaloids in Schedule I, the most restrictive and punitive schedule, of the Controlled Substances Act, but a group of scientists has urged that this could have dire consequences for kratom users. Lastly, to some scientists, the recent kratom-linked *Salmonella* outbreak signals the need for quality control, not a federal ban.

62 Herbal Supplement Sales in US Increase 8.5% in 2017, Topping $8 Billion
By Tyler Smith, Kimberly Kawa, Veronica Eckl, Claire Morton, and Ryan Stredney

In 2017, US retail sales of herbal dietary supplements increased by 8.5%, or roughly $633 million, from the previous year, reaching an estimated total of $8.085 billion. This is the strongest sales growth for these products in more than 15 years and marks the first time that US consumer spending on herbal supplements has surpassed $8 billion. The 2017 *HerbalGram* Herb Market Report is based on data supplied by the market research firms SPINS and IRI, both based in Chicago, Illinois, and the *Nutrition Business Journal*, part of the New Hope Network, a natural products industry-focused media company based in Boulder, Colorado. Sales in both mainstream and natural retail channels were bolstered by increased consumer interest in Ayurvedic herbs such as turmeric (*Curcuma longa*, Zingiberaceae) and ashwagandha (*Withania somnifera*, Solanaceae), as well as the continued appeal of botanicals with general health benefits and those in non-pill forms, such as powders and liquids.

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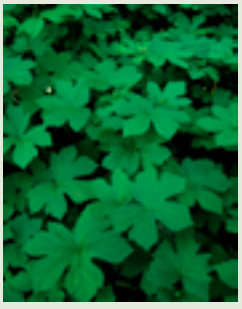
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American Ginseng (*Panax quinquefolius*, Araliaceae)



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Goldenseal *Hydrastis canadensis*
Photo ©2018 Steven Foster

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Grape Seed

Vitis vinifera

Family: Vitaceae

INTRODUCTION

The Vitaceae or grape family includes about 900 species in 15 genera. About 70 interfertile (capable of interbreeding) species compose the genus *Vitis*. Of these, *V. vinifera* is the best known, as well as the most culturally and economically important.[1] *Vitis vinifera* originated in central Asia, but it now occurs in many regions of the world as a result of extensive cultivation and escape.[2] It is a perennial liana (woody, climbing vine) that climbs with coiled tendrils. Grapes were among the first fruits to be domesticated thousands of years ago, and there are currently an estimated 10,000 cultivars of this single species. The domesticated subspecies *V. vinifer*a subsp. *vinifera* (syn. *V. vinifera* subsp. *sativa*, or *V. sativa*) is monoecious (hermaphroditic), having both male and female reproductive organs in a single individual. It descended from a wild ancestor *V. vinifera* subsp. *sylvestris* (syn. *V. sylvestris*), which is dioecious — having male and female reproductive organs in separate individuals. The subspecies *sylvestris* now occurs in the wild from the Atlantic coast of southwestern Europe to Tajikistan and the western Himalayas in central and southern Asia.[3] More than 90% of the world production of grapes is from *V. vinifera*.[4] However, other *Vitis* species, including *V. berlandieri*, *V. riparia*, and *V. rupestris*, are used as germplasm resources to breed rootstock for improved resistance against fungal diseases.[5] Other *Vitis* species used for wine production, in particular *V. labrusca*, also provide seed material for the production of grape seed extract (GSE*).[6]

GSEs typically are produced from dried or fresh grape seeds that are obtained as a byproduct of the juice and wine industries. First, the grape seeds are extracted using a solvent (e.g., water, or mixtures of water with ethanol or acetone) and then filtered and subjected to further processing in order to produce GSE that contains anywhere from 50% to 90% phenolic compounds.[7] There is also a pharmacopeial GSE called "Grape Seeds Oligomeric Proanthocyanidins," defined in the *United States Pharmacopeia* (USP) as the fraction of an extract of the ripe seeds of *V. vinifera* containing not less than 75.0% oligomeric proanthocyanidins (OPCs).[8]

HISTORY AND CULTURAL SIGNIFICANCE

The Latin genus name *Vitis* means "grape vine," while the species name *vinifera* means "produces wine" or "wine bearing"" and is related to the Latin terms *vinum* ("wine") and *vinea* ("vineyard").[9] The words "wine," *vin* (French), and *Wein* (German) stem from the ancient Greek term οινος (oinos) and the Latin term *vinum*.[10]

Swedish botanist Carl Linnaeus (1707-1778) included *Vitis vinifera* in his 1749 work *Materia Medica* and described its occurrence as "*orbis totus temperatus*" (global, temperate). For therapeutic use, he did not describe the seed but rather the leaf (as Vitis Folia), stating that it was used to treat stranguria (slow, painful urination) and tussis (cough).[11]

Grape is considered a "cultural keystone species" and is associated with divinities and rituals, evidenced by representations on artifacts of ancient cultures of the Mediterranean.[12] Archaeobotanical evidence of *Vitis* species is mainly in the form of waterlogged, mineralized, and charred seeds. It is difficult to determine whether these seeds originated from wild or cultivated plants[13] because the seeds of *V. vinifera* subsp. *sylvestris* (wild) and *V. vinifera* subsp. *vinifera* (cultivated), for example, are morphologically very similar.[14] Domestication of the cultivated grape reportedly took place between the seventh and the fourth millennia BCE in the Caucasus region (between the Black Sea and the Caspian Sea) in present-day Georgia, Armenia, and Azerbaijan,[5,15] where the crop exhibits high genetic diversity. From the Caucasus, cultivation is believed to have spread to Mesopotamia and Egypt and then throughout the Mediterranean[16] and beyond. Approximately 9,000-year-old grape pips (seeds) found in the southern Caucasus provide the earliest known archaeological evidence of grape cultivation.[17] Based on botanical, ampelographic (the science concerned with identification and classification of grape vines), archaeological, paleontological, historical, ethnographical, and linguistic studies, Georgia is recognized as one of the earliest sites



Grape *Vitis vinifera*
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* The acronym GSE should not be confused with the acronym GFSE, which refers to grapefruit (*Citrus paradisi*, Rutaceae) seed extract, an entirely different material. In some original publications on GFSE adulteration, the authors use "GSE" to refer to grapefruit seed extract.

of grape domestication.[18] Today, the most widely cultivated species in Georgia are *V. vinifera* and *V. labrusca* and their varieties, including *V. labrusca* var. *izabella* (purple), *V. vinifera* var. *Rkatsiteli* (white), and *V. vinifera* var. *Saperavi* (red). The fermented grape seed residue byproduct of these species are being studied in Georgia as potential source materials for commercial production of GSE.[6]

While there are well-documented traditional medicinal uses of other plant parts of *V. vinifera* — for example, the dried leaf (pharmacopeial name: Vitis viniferae folium),[19] the dried fruit or raisin (Uvae passae or Vitis viniferae fructus), and processed forms such as wine (Vinum)[20] — extraction of the seed for functional, nutritional, or therapeutic uses is a relatively new innovation. Development of GSE traces back to research begun in the late 1940s, although commercial products did not appear until the 1970s. In 1947, French scientist Jack Arthur Masquelier (1922-2009) extracted a colorless fraction from peanut (*Arachis hypogaea*, Fabaceae) skin, proposing that its major components were oligomers of flavan-3-ol units (e.g., (+)-catechin or (-)-epicatechin), which today are classified as oligomeric flavan-3-ols. Over the decades, this led to research into other potential sources of the compounds, including pine (*Pinus* spp., Pinaceae) bark and grape seed. By 1970, Masquelier had isolated these flavanols from grape seeds[21] and applied for a patent for his extraction process, which was granted to his company, Société Civile d'Investigations Pharmacologiques d'Aquitaine (SCIPA), in 1972 by the French National Institute of Industrial Property (INPI).[22] Today, GSE is used as a component of dietary supplement products and natural health products for venous insufficiency (in which veins have problems sending blood from the legs back to the heart), to promote wound healing, and to reduce inflammation.[23] It is also used as a functional food additive and cosmetic ingredient.

In 2003, San Joaquin Valley Concentrates (Fresno, California) submitted a Generally Recognized as Safe (GRAS) notice to the US Food and Drug Administration (FDA) for a GSE to be used as an antioxidant or emulsifier component of food products at levels ranging from 0.01% to 0.08%. The FDA responded that it had no questions regarding San Joaquin's conclusion that GSE is GRAS under the intended conditions of use.[24] In the same year, Polyphenolics, Inc. (Madera, California) submitted a GRAS notice for GSE and grape pomace extract (GPE) for use as antioxidants in certain fruit beverages at a concentration of up to 210 parts per million (alone or in combination with other ingredients). Again, the FDA had no questions regarding Polyphenolics' conclusion that GSE and GPE are GRAS under the intended conditions of use.[25] Subsequently, in 2007, Polyphenolics, Inc. requested and received an independent GRAS extension expert opinion that justified increasing the concentration in beverages to up to 845 mg/L (200 mg/8 oz). Enovita, a GSE from Indena (Milan, Italy), is also GRAS as per an independent GRAS assessment and conclusion (G. Ris email to T. Smith, June 18, 2018).

In 2008, a new dietary supplement quality standards monograph titled "Grape Seeds Oligomeric Proanthocyanidins" was proposed for entry into the USP. A draft monograph was published in the *Pharmacopeial Forum* for public comment,[26] after which the final monograph became official in the 33rd revision of the USP in 2010.[27]

In 2012, the company Nutrilinks Sarl (Lausanne, Switzerland) submitted an application to the European Food Safety Authority (EFSA) for an opinion on scientific substantiation of its proposed health claim for GSE related to maintenance of normal venous blood flow. The subject of its application was a dry extract obtained by extraction of grape seeds with ethanol and ethyl acetate, and subsequent evaporation, filtration, concentration, and spray-drying, standardized to total polyphenol content (minimum 35% of gallic acid, catechins, and epicatechins, and minimum 7% of procyanidin dimers B1, B2, B3, and B4). The EFSA concluded that the data did not establish a cause-and-effect relationship between the consumption of this GSE and maintenance of normal venous blood flow.[28] Another application by the same company was submitted to the EFSA in 2012 for an opinion on scientific substantiation of a health claim for its



Grape
Vitis vinifera
Photo ©2018 Steven Foster

GSE related to the elimination of excess water in the body. The EFSA panel concluded that the applicant's proposed claim statement ("helps to drain the body in case of water accumulation") in the context of "normal venous circulation in the legs" refers to the maintenance of normal venous blood flow, and that a claim for GSE and maintenance of normal venous blood flow had already been assessed and rejected.[29]

CURRENT AUTHORIZED USES IN COSMETICS, FOODS, AND MEDICINES

In the United States, GSE is classified as GRAS for certain limited food uses and appears on the FDA's list of "Substances Added to Food" (formerly "Everything Added to Food in the United States," or EAFUS).[30] GSE may also 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).[31] In Canada, GSE standardized to 80-85% OPCs 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). Depending on the dosage and strength, labels of licensed GSE NHPs may carry one or both of the following claim statements: "Source of antioxidants for the maintenance of good health" and "Helps to relieve symptoms related to non-complicated chronic venous insufficiency (CVI), such as sensation of swelling, heaviness and tingling of the legs."[32]

In the European Union, different types of GSE are listed as components of cosmetic products and are used for various functions (e.g., antidandruff, antimicrobial, antioxidant, oral care, skin-protecting, and UV-absorbing functions). "Oleoyl GSE" (obtained by the reaction of oleoyl chloride with GSE), "Propyl Oleoyl GSE" (obtained by the reaction of oleoyl chloride with the propyl ether of GSE), and "Undecylenoyl GSE" (obtained by the reaction of GSE with undecylenoyl chloride) are all used for antioxidant function; "Palmitoyl GSE" (GSE reaction products with hexadecanoyl chloride) is used for skin-conditioning function; and "Sodium GSE Phosphate" (sodium salt of a complex mixture of esters of phosphoric acid and GSE) is used for antioxidant and skin-conditioning functions.[33]

MODERN RESEARCH

Proanthocyanidins (PACs) are the major chemical compounds in GSEs. The PAC content of GSEs typically comprises 5-30% monomers (including catechins, epicatechins, and other flavan-3-ol monomers), 17-63% oligomers,† and 11-39% polymers (and their gallic acid esters). GSEs contain primarily B-type PACs (flavan-3-ol polymers where the units are linked by a single bond). The large number of grape varieties used to make GSEs accounts for the varied concentrations of bioactive chemical compounds in the seeds.[7,34]

There are a number of clinical studies on various GSEs for numerous conditions and functions, such as atherosclerosis prevention,[35,36] chronic periodontitis,[37] climacteric syndrome,[35] estrogen levels,[38] hyperlipidemia,[36,39,40] hypertension,[41,42] idiopathic male infertility,[43] leg swelling during prolonged sitting,[44] liver function,[45] oxidative stress and reperfusion injury caused by cardiopulmonary bypass surgery,[46] postprandial oxidative stress and inflammation in persons with metabolic syndrome,[47] postprandial blood glucose,[48] renal failure in chronic kidney disease,[49] antioxidant capacity and lipid peroxidation in type 2 diabetes mellitus,[50] and skin protection from UV radiation.[51] Most of these studies are of varying degrees of quality and, while they all show some positive outcomes, they are either preliminary studies; were not randomized, double-blind, and placebo-controlled (RDBPC); did not explain randomization, blinding, or withdrawals; and/or had a very small study population.

One recent RDBPC study investigated the effects of GSE supplementation on oxidative stress and metabolic profiles of female volleyball players. Forty healthy volunteers (14-24 years old) were randomly assigned to take 300 mg GSE (formulated by Barij Essence Pharmaceutical Co.; Kashan, Iran; no additional information provided) or placebo twice a day, with lunch and dinner, for eight weeks. Participants kept dietary records on one weekend day and two weekdays, and physical activity records on weeks two, four, and six of the study. Fasting blood samples were obtained before and after the intervention and centrifuged, and the total antioxidant capacity (TAC), total glutathione (GSH, an antioxidant), malondialdehyde (MDA, a marker of oxidative stress), nitrous oxide (NO), creatine phosphokinase (CPK), fasting plasma glucose (FPG), serum triglycerides, serum insulin, and very low-density lipoprotein (VLDL), low-density lipoprotein (LDL), high-density lipoprotein (HDL), and total cholesterol levels were measured. The GSE group experienced a significant increase in GSH compared to placebo, and a significant decrease in MDA compared to placebo. Additionally, GSE supplementation resulted in decreased serum insulin concentrations, decreased scores on the homeostasis model assessment for insulin resistance index, and increased scores on the quantitative insulin sensitivity check index compared to placebo, all of which are considered beneficial effects on insulin metabolism. There were no significant changes in CPK, TAC, NO, FPG, or serum lipid concentrations compared to placebo.[52]

Two meta-analyses have reported on clinical studies investigating the effects of GSE on cardiovascular risk markers. The first, conducted in 2011, included nine randomized, controlled trials published between 2000 and 2009 (N = 390) that focused on at least one of the following: systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate, triglycerides, C-reactive protein (CRP), or total, LDL-, or HDL-cholesterol. This meta-analysis concluded that GSE supplementation was associated with significantly lowered SBP and heart rate with no signifi-

† The authors define oligomers as PACs that have 2-7 units.

cant effects on DBP, CRP, or serum lipid levels. While the reduction in SBP was modest compared to that seen with prescription antihypertensive drugs, it may still be meaningful since it is estimated that "every 3 mm Hg reduction in SBP could reduce the risk of all-cause mortality by 4%, mortality after stroke by 8%, and mortality after coronary artery disease by 5%." The authors opined that GSE might have cardioprotective effects beyond SBP and heart rate reductions, and that larger studies should be done evaluating different dosages of GSE with longer follow-up durations.[53]

A more recent meta-analysis from 2016 included 12 articles (16 randomized trials, N = 810) that analyzed the effects of GSE on blood pressure over at least two weeks. Of the 16 clinical trials, four studied GSE's effects in patients with prehypertension and stage 1 hypertension, four included healthy subjects, three in patients with metabolic syndrome, two in patients with hypertension, two in women with at least one menopausal symptom, and one in patients with above-average vascular risk. Overall, GSE was associated with significant changes in SBP and DBP. Significant decreases in SBP and DBP occurred more often in subjects under 50 years of age, while significant decreases in SBP alone occurred in obese subjects and patients with metabolic syndrome. Additionally, the authors identified study design, randomization, and baseline blood pressure as possible causes of heterogeneity (variability between the studies). Therefore, they recommend confirmation of their findings through a "large-scale, long-term, multiple-dose randomized controlled trial, especially among hypertensive patients."[54]

At least seven clinical trials have studied GSE in combination with other ingredients for a variety of uses. Five of these addressed skin conditions. One found that skin radiance (e.g., for pink and olive skin tones) was significantly improved with six weeks of oral treatment with 150 mg per day of SkinAx^2 (a product containing GSE, superoxide dismutase-rich melon [*Cucumis melo* var. *cantalupensis*, Cucurbitaceae] concentrate, vitamin C, and zinc; Activ'Inside; Libourne, France).[55] Another oral supplement with 27.5 mg GSE, 210 mg biomarine complex, 54 mg vitamin C, 4 mg zinc, and 28.76 mg tomato (*Solanum lycopersicum*, Solanaceae) extract (Imedeen Man. Age.Ment; Ferrosan Laboratórios S/A; Copenhagen, Denmark) taken twice a day for 30 days improved skin hydration, dermal ultrasound density, reduction of skin pH, and overall signs of skin aging in men.[56] Likewise, an oral supplement (Imedeen Time Perfection; Ferrosan S/A; Copenhagen, Denmark) with 105 mg BioMarine Complex, 14.8 mg LycoPhence GS (lycopene and GSE), and 30 mg acerola (*Malpighia* spp., Malpighiaceae) taken for 120 days was associated with improvements in skin hydration and pH, ultrasound density, and a histological increment of collagen and elastic fibers.[57] An SPF 30 sunscreen containing GSE, vitamins E and C, and ubiquinone (Dr. Peter Hansen R&D; Stada; Bad Vilbel, Germany) effectively protected the subjects' skin against infrared A radiation.[58] Finally, a nonsteroidal topical cream (MD2011001; no other information provided) containing GSE, vitamin E, and epigallocatechin gallate (EGCG) provided a faster and statistically significant improvement in atopic dermatitis in patients who used it for 28 days, compared to placebo.[59]



Grape
Vitis vinifera
Photo ©2018 Steven Foster

One RDBPC study investigated the benefits of a nutritional supplement in low-income patients recently diagnosed with hyperlipidemia (N = 191; 18-65 years old). Subjects were randomly assigned to receive a placebo or a proprietary phytonutrient supplement (PreLipid; Preventions Meds, Inc.; Lebanon, NJ; no additional information provided) containing red yeast rice (a product of a yeast [*Monascus purpureus*, Elaphomycetaceae] grown on white rice [*Oryza sativa*, Poaceae]) powder, GS powder, niacin, folic acid, and black pepper (*Piper nigrum*, Piperaceae) powder. Subjects taking PreLipid experienced significant reductions in LDL-C and non-HDL-C at 12 weeks compared to placebo.[60]

Another RDBPC study investigated the effects of 150 mg GSE (MegaNatural BP; Polyphenolics; Madera, CA) in a fruit juice blend (provided by Coca-Cola) on blood pressure and metabolic indices in men and women with prehypertension (N = 28; 25-65 years old). Subjects were randomly assigned to take placebo or 300 mg GSE/juice blend per day in two doses for 12 weeks. By week six, the GSE group experienced significantly reduced SBP (5.6%) and DBP (4.7%) compared to placebo. The higher the subjects' baseline BP, the greater the reduction they experienced; in some cases, subjects taking the GSE/juice blend experienced nearly double the SPB and DBP reduction of those in the placebo group. While not significant, fasting insulin and insulin sensitivity of subjects in the GSE/juice blend group tended to improve after six weeks.[61]

FUTURE OUTLOOK

The International Union for Conservation of Nature (IUCN) assigns wild *V. vinifera* to the conservation category of Least Concern (LC), meaning that the species is not considered to be threatened.[2] In any case, GSE is produced from seeds of the widely cultivated grape that is used for production of juices and wines worldwide. Nonetheless, long-term survival of crop wild relatives remains critical for preserving genetic diversity. Some wild grape species are becoming threatened in Europe due to habitat loss, competition with alien grape species, and intensive deforestation.[62]

Perhaps the biggest concern is economic adulteration of GSE, which has a direct impact on its safety and efficacy. In 2016, the American Botanical Council (ABC)-American Herbal Pharmacopoeia (AHP)-National Center for Natural Products Research (NCNPR) Botanical Adulterants Prevention Program published a Botanical Adulterants Bulletin on GSE, reporting that "adulteration of GSE in commercial products appears to be a significant problem." In one of the studies cited in the bulletin, samples of several commercial GSE products contained no GSE at all and were composed primarily of peanut skin extract. Although peanut skin extracts should not exhibit allergenic potential comparable to that of peanuts themselves (due to no protein content), allergenicity could still be possible due to contact with the peanut protein. Besides the obvious matter of consumer fraud, persons with peanut allergies who unwittingly consume these products could experience adverse reactions. Other known adulterants of GSE include pine bark, green tea (*Camellia sinensis*, Theaceae) extract, and other PAC-rich (e.g., propelargonidin-containing) extracts from non-grape seed sources.[7]

While GSE is a relatively new item of commerce, evidence that supports its various beneficial uses as a functional component of cosmetic, food, dietary supplement, and natural health products continues to grow. To ensure the safety and efficacy of GSE for its intended uses, all finished product brands and marketers should specify the production and procurement of only well-characterized GSE for use in consumer products. For example, the USP quality standards monograph Grape Seeds Oligomeric Proanthocyanidins provides a useful basis for a company to establish a scientifically valid specification with suitable tests and methods for verifying identity, composition, strength, and purity. HG

—Gayle Engels and Josef Brinckmann

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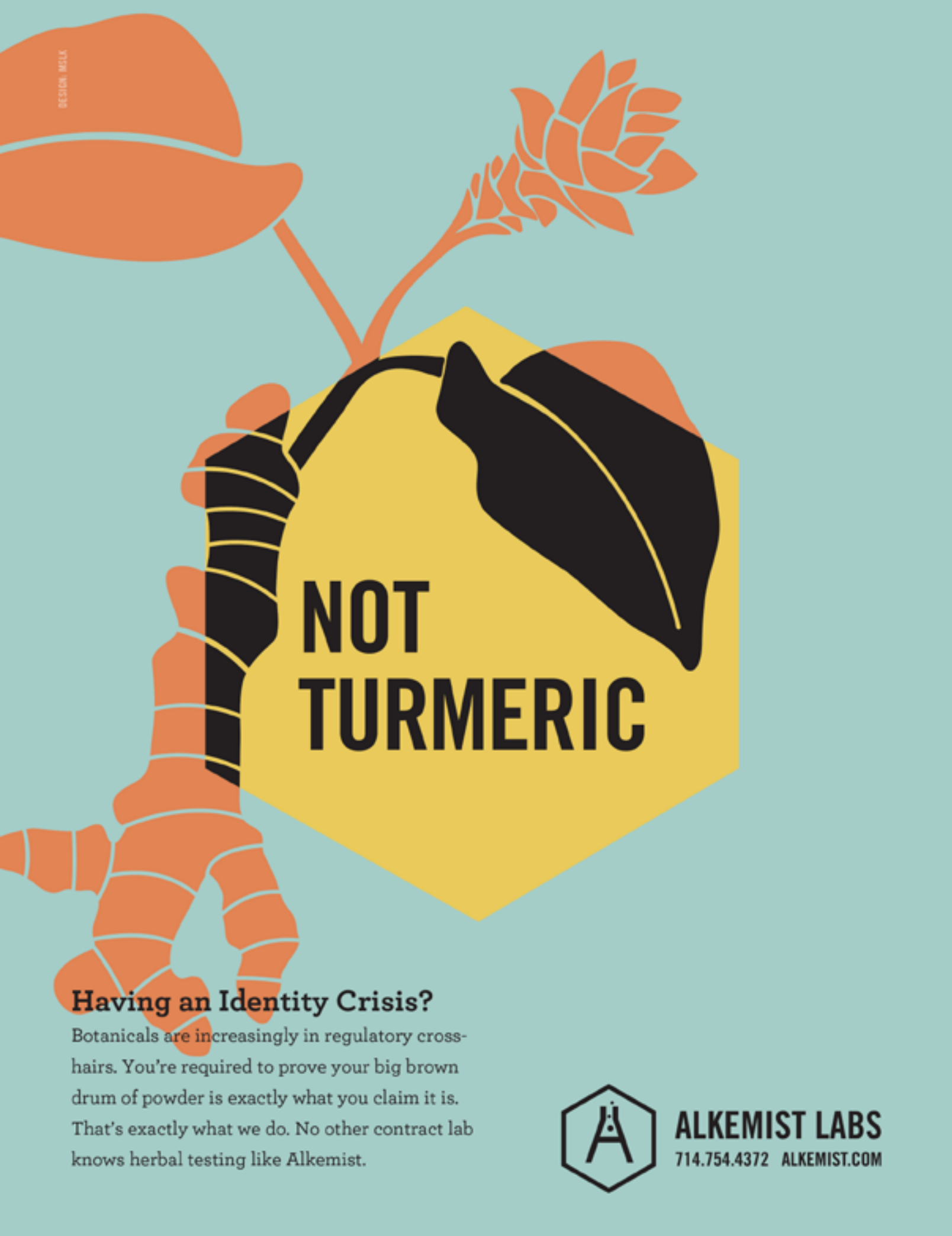
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HERBALGRAM
Celebrates 35 Years of Publication

ABC's flagship magazine noted internationally for quality, reliability, and beauty in reporting on medicinal plants

August 2018 marks the 35th anniversary of *HerbalGram*, the quarterly journal of the American Botanical Council (ABC). Since its first issue in 1983, *HerbalGram* has transformed from a black-and-white newsletter to a full-color, 82-page journal with the visual appeal of beautiful botanical photography and intellectual draw of peer-reviewed articles. Though *HerbalGram* has evolved significantly, its editorial mission to serve as a reliable herbal education resource has remained the same.



Issue #20

Issue #61


Issue #10



Issue #30



Issue #36



Issue #46

In the summer of 1983, ABC Founder and Executive Director Mark Blumenthal produced the first issue of *HerbalGram*, which was then titled "Herb News" with the subtitle "Herbalgram." Blumenthal, who also was running his former herb distribution business, Sweethardt Herbs, spent many of his nights and weekends collecting, writing, and editing articles for the newsletter. It was this focus on disseminating trustworthy and timely herbal information that would eventually lead Blumenthal to found ABC in 1988.

Originally published with financial support from the newly formed American Herbal Products Association (AHPA), of which Blumenthal was a founding board member, the first *HerbalGram* was an eight-page, black-and-white newsletter stapled at the spine. It consisted of "herb blurbs" on herbal miscellanea, a "media watch" section with herb-related news articles, a handful of paragraph-long "Rob's Research Reviews" authored by then-Associate Editor Robert McCaleb (who, at the time, was also head of research at Celestial Seasonings), listings of herbal information resources and schools, and more. The editorial staff included just Blumenthal and McCaleb, who also co-founded the Herb Research Foundation (HRF) together.

For the second issue, Blumenthal enlisted two additional part-time assistant editors. The publication now featured the title "Herbalgram" in larger font. This issue took on a more defined format, with organized sections on industry news, conferences/meetings, HRF news, and "potpourri" — a catch-all section featuring various news items of possible interest to the growing herbal industry and community.

In the following years, *HerbalGram* transformed into a modern force in the botanical medicine community. In 1988, *HerbalGram* issue 18/19 was the first color edition with a cover illustration of St. John's wort (*Hypericum perforatum,* Hypericaceae). This 48-page double issue also was the first published under the auspices of both HRF and ABC, which Blumenthal founded with the late ethnobotanist James A. Duke, PhD, and the late Professor Norman Farnsworth, PhD, in order to help transition the publication from newsletter to journal. In 1992, issue 28 was the first full-glossy, four-color issue, and featured an image of the Ware Collection of Blaschka Glass Models of Plants from the Harvard Museum of Natural History on the cover. The journal increased to its current length of 82 pages in 1999, and, in 2000, issue 50 was the first to be published by ABC alone.

Eighteen years and almost 70 issues later, the editorial staff of *HerbalGram* has grown to include an art director and three full-time editors, in addition to Blumenthal, who serves as editor-in-chief, along with many other employees at ABC who serve in a variety of other important roles. The journal features articles both from in-house writers and

botanical experts from around the world, and all are peer-reviewed by members of ABC's distinguished advisory board or other professionals with relevant expertise. *HerbalGram* reaches thousands of readers in more than 81 countries who represent a range of diverse professions, from research scientists (e.g., pharmacognosists, ethnobotanists, etc.) and health practitioners (e.g., herbalists, naturopathic physicians, pharmacists, conventional physicians, etc.) to industry members, government regulators, and many others.

HerbalGram has been a leader in presenting extensive literature reviews on specific herbs in an effort to help establish a scientific basis for their potential health benefits. In some cases, these reviews can also help clarify erroneous or inappropriate claims about the uses of the herbs.

"*HerbalGram* has served as the go-to source for detailed perspectives on developing herb-related topics for 35 years," said Steven Foster, an herbalist, photographer, author, and ABC Board of Trustees member. "The publication is at the forefront of covering topics such as herb conservation and the effect of climate change on herb crops, clear assessments of regulatory and market developments, as well as emerging science."

Foster added: "The depth of coverage, detailed quality of presentation, rigorous peer-review process, meticulous editorial attention, aesthetic beauty, and broad appeal [of *HerbalGram*] combine to reach a standard of lasting excellence that few science-based periodicals achieve."

Recent *HerbalGram* issues have featured significant articles such as issue 118's pictorial on Joseph Banks' historic Florilegium of botanical life that was encountered on Captain Cook's first South Pacific voyage; issue 116's beautiful and informative deep-dive into medicinal trees of North America; and issue 103's feature about the effects of climate change on the quality of tea.

Each year, *HerbalGram* also publishes its annual Herb Market Report, which describes the trends of the botanical dietary supplement market in the United States and frequently is cited in other publications. Additional in-depth key articles published in recent issues have included a look into the history and pharmacology of the emerging Southeast Asian tree kratom (*Mitragyna speciosa*, Rubiaceae); a pet supplement herb market report; notes from a 17th-century ethnobotanical expedition to South Africa; and many more.

Issue #52



Issue #66





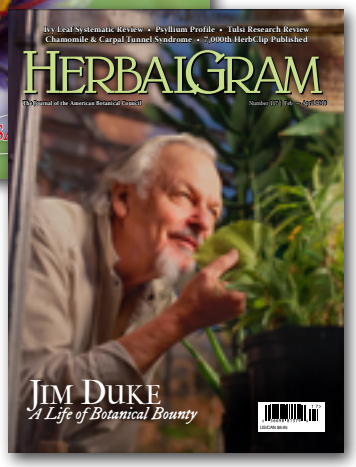
Issue #77



Issue #84



Issue #110



Issue #117

Loren Israelsen, president of the United Natural Products Alliance, praised *HerbalGram*'s diverse content. "When my *HerbalGram* arrives in the mail, I know I will begin another journey into the wonders of the herbal kingdom," he said. "While I no longer save other magazines, I treasure and hold tight to my copies of *HerbalGram*. I, along with many others, salute ABC and *HerbalGram* for its 35 years of service to the advancement of consumer, industry, and professional education, high level of professionalism, and documenting the rich history of our remarkable community."

In November 2011, the ABC-AHP-NCNPR Botanical Adulterants Prevention Program (BAPP) published its first feature-length article — "A Brief History of Adulteration of Herbs, Spices, and Botanical Drugs" — in *HerbalGram* issue 92. The article, written by Foster, reviewed numerous cases of adulterated, fraudulent foods, spices, and drugs during the past two millennia. *HerbalGram* also has published extensively peer-reviewed BAPP feature articles on the adulteration of bilberry (*Vaccinium myrtillus,* Ericaceae) extract, skullcap (*Scutellaria lateriflora,* Lamiaceae) herb, so-called "grapefruit seed extract," and black cohosh (*Actaea racemosa*, Ranunculaceae) in addition to Foster's epic 22-page article, titled "Toward an Understanding of Ginseng Adulteration: The Tangled Web of Names, History, Trade, and Perception."

In 2012, ABC introduced an online "page-flip" version of *HerbalGram* that is optimized for viewing on smartphones, tablets, and computers. In 2016, all issues of *HerbalGram* became available in PDF format, from 1983's issue 1 through the current issue, thanks to a digitizing project overseen by Art Director Matt Magruder in 2016. Before that, only issues 85 and above were available as PDF files.

HerbalGram is available as a benefit of ABC membership at the Individual level and up. It also is sold in some bookstores and natural food stores.

—ABC Staff

American Botanical Council Submits Comments to FDA Suggesting Rescheduling of Cannabis

ABC highlights clinical research supporting therapeutic benefits, noting that current Schedule I status significantly impedes research efforts on cannabis, cannabis preparations, and its compounds

The American Botanical Council (ABC) recently submitted comments to the US Food and Drug Administration (FDA), noting "that more clinical and other research into the medicinal properties of cannabis is warranted, and that the Schedule I status of cannabis is one of the most significant impediments to carry out such research."[1]

ABC's submission was in response to the FDA's request for "comments concerning abuse potential, actual abuse, medical usefulness, trafficking, and impact of scheduling changes on availability for medical use" of five substances: cannabis plant and resin; extracts and tinctures of cannabis; delta-9-tetrahydrocannabinol (THC); stereoisomers of THC; and cannabidiol (CBD).[2]



Cannabis
Cannabis sativa
Photo ©2018 Steven Foster

The US Department of Health and Human Services took the public comments into consideration as it prepared its response to a request for information from the World Health Organization (WHO). According to the FDA, the WHO "will use this information to consider whether to recommend that certain international restrictions be placed on these drugs."[2] The WHO conducted a "pre-review" of the evidence submitted by member countries during a special session on cannabis and cannabis-related substances at the 40th meeting of the Expert Committee on Drug Dependence held in June 2018. The WHO is expected to present its final report and recommendations in late July.[3]

In its comments, ABC emphasized that cannabis' Schedule I status under the Controlled Substances Act of 1970 is outdated and inappropriate. A Schedule I drug or substance is defined as having "a high potential for abuse," "no currently accepted medical use in treatment in the United States," and "a lack of accepted safety for use … under medical supervision."[4]

"In 1970, when the Controlled Substances Act was enacted, reliable information on the medical value of cannabis was relatively scarce," ABC noted.[1] "This has changed over the past years, where a number of clinical studies have been carried out to evaluate cannabis, and cannabis isolates, for a variety of conditions and ailments."

In the comments sent to the FDA, ABC provided short summaries with evidence of the benefits of cannabis, and cannabis fractions enriched in CBD, or THC and CBD, as therapeutic agents in the treatment of pain, multiple sclerosis, and epilepsy. The included data are based on a literature review, which summarized a number of systematic reviews and meta-analyses published between 2015 and 2018. The publications substantiate that cannabis preparations have significant medical benefits.

In June 2018, approximately two months after ABC submitted its comments, the FDA approved the CBD oral solution Epidiolex (GW Pharmaceuticals; Cambridge, United Kingdom) for the treatment of two rare forms of childhood epilepsy. This is the first time the administration has approved a cannabis-derived drug.[5]

ABC concluded: "Based on the promising results from the human studies on cannabis, the current hurdles to investigate cannabis, cannabis extracts, and purified fractions obtained from cannabis ... do not seem appropriate in view of the potential benefits that this plant might provide. Therefore, [ABC] recommends that cannabis be removed from Schedule I [of] the Controlled Substances Act and that other appropriate actions are undertaken to enable more appropriate access of cannabis and its components for medicinal investigations."[1]

A copy of ABC's comments, which were written by ABC Chief Science Officer Stefan Gafner, PhD, is available at www.herbalgram.org. HG

—ABC Staff

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Four Elements Adopts Lemon Balm through ABC's Adopt-an-Herb Program

The American Botanical Council (ABC) recently welcomed Four Elements Organic Herbals' adoption of lemon balm (*Melissa officinalis*, Lamiaceae) through ABC's Adopt-an-Herb botanical education program.

Four Elements' adoption supports ABC's extensive HerbMedPro database, ensuring that this essential educational resource remains current for researchers, health professionals, industry, students, consumers, and other members of the herbal and dietary supplements community.

ADOPT-AN-HERB HerbMedPro™ PROGRAM

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 250 herbs, spices, and medicinal plants.

"When ABC started the Adopt-an-Herb program, I thought *Melissa officinalis* should be represented, almost like a parent likes to see his or her child honored for doing well," wrote Jane Hawley Stevens, the founder of Four Elements. "I hope when people see Four Elements' logo with *Melissa officinalis*' photo, they are reminded that the plant has many benefits (calming, antiviral, joy-enhancing, carminative, and more) while being delicious, abundant, and easy to grow. They should be reminded to drink some lemon balm tea!"

"I feel such deep gratitude for plants and nature in general, and for all the healing potential provided in these aromatic, beautiful packages," Stevens continued. "Honoring my favorite herb, lemon balm, through this organization, helps to fulfill my mission of connecting plants to people to increase wellness for the people and the planet. I am happy to help support an organization that actively gathers and brings forth herbal research for the good of all. It brings me joy to now claim the nickname 'Mother of *Melissa*,' having adopted her through this worthy ABC program, fortified with my 2,000 *Melissa officinalis* plants in my field I started from seed!"

About Lemon Balm

Native to southern Europe, lemon balm is a bushy perennial that can grow to two or three feet tall. Like other members of the mint family, it has square stems and opposite, branching leaves. The flowers, which usually appear from about June to September, are small, inconspicuous, yellow to pinkish-white, and have the "lipped" look typical of the mint family. Unlike many members of the mint family, the plant's roots are not invasive.

The leaves smell like lemon (*Citrus* × *limon*, Rutaceae) when bruised or crushed, hence the plant's common name. When fresh, they may be used in drinks and added to salads, soups, sauces, and vegetables. When dried, they may be used to flavor teas and added to sachets and potpourris. Lemon balm reportedly is one of the few sour-tasting mints.

In his *Historia Plantarum*, the Greek philosopher and botanist Theophrastus of Eresus (372-287 BCE) provided one of the first known descriptions of the plant. It is thought that the idea of "Carmelite Water," or *Eau de Carmélite*, an alcoholic extract of lemon balm and other herbs, originated in about 1200 when Christian hermits living in caves on Mount Carmel in present-day Israel realized the benefits of lemon balm. It is also widely believed that the "balm" of Homer's *Odyssey* and Shakespeare's *Merry Wives of Windsor* refers to lemon balm. In addition, Thomas Jefferson reportedly cultivated the species at Monticello.

Traditionally, lemon balm has been used to calm nervous disorders, alleviate insect bites, increase perspiration, and treat colds, gastrointestinal and sleep disorders (including insomnia), and fevers. Preparations of the plant have demonstrated antimicrobial, antioxidant, antispasmodic, antiviral, bacteriostatic, neuroprotective, pain-relieving, and sedative effects. The plant contains phenolic acids (primarily rosmarinic acid), flavonoids, and essential oil (with citronellal, neral, and geranial as the predominant compounds).

Lemon balm produces abundant nectar and is highly favored by bees. In fact, the genus name *Melissa* is Greek for "honeybee" or "bee." In Greek mythology, Melissa was a nymph who discovered how to obtain honey, and, in one version of the myth, was transformed into a bee by Zeus. In the fourth book of Virgil's *Georgics*, from the first century BCE, the Roman poet wrote about "baum" (likely lemon balm) as a bee attractant. And, in 1629, English herbalist John Parkinson wrote: "It is also an herbe wherein bees doe much delight." When bees swarm, usually in the spring and when the hive becomes overcrowded, the queen leaves the hive with about 50-60% of her offspring to establish a new brood-rearing colony elsewhere. Beekeepers can lose thousands of bees to swarming. Lemon balm has been used effectively (spread inside bait boxes or bait hives) to capture swarms, including feral swarms, and prevent loss of bees.

More information about lemon balm can be found on the lemon balm adoption page in ABC's HerbMedPro database and its HerbMedPro record.

About Four Elements

Established in 1987, Four Elements offers a variety of herbal wellness products (including arnica [*Arnica montana*, Asteraceae] cream, soaps and body lotions, herbal tinctures,

FOUR ELEMENTS

Lemon Balm

Melissa officinalis

and herbal teas) that are created and packaged at its farm in the Baraboo Bluffs of Wisconsin. The company is dedicated to growing organic, and has been certified since 1990.

About Adopt-an-Herb and HerbMedPro

Four Elements is one of 57 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 fungi-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, 62 herbs have been adopted.

Each adopted herb is continuously researched for new scientific articles and 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 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



Lemon balm
Melissa officinalis
Photo ©2018 Steven Foster

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.

One of the benefits of supporting the Adopt-an-Herb Program is that it ensures that the most current information on the adopted herb is available through ABC's powerful HerbMedPro™ database.

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 120, or by email at denise@herbalgram.org.

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	Tongkat Ali *Eurycoma longifolia*
lafn USA	**Monk Fruit** *Siraitia grosvenorii*
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CONTAINS Zembrin	**Sceletium** *Sceletium tortuosum*
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YOUR LOGO	**Plant name** *Scientific name*

Become an adopter today!

BAPP Publishes Adulterants Bulletins on Turmeric Extracts and Boswellia Resin

The ABC-AHP-NCNPR Botanical Adulterants Prevention Program (BAPP) has released Botanical Adulterants Bulletins on turmeric (*Curcuma longa*, Zingiberaceae) rhizome and its extracts and boswellia (*Boswellia serrata*, Burseraceae) oleogum resin,* commonly referred to as frankincense. Both herbs are popular in the traditional medicine systems of India.

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

Turmeric Bulletin Focuses on Adulteration with Related Species, Artificial Colorants, and Synthetic Curcuminoids

Few herbal dietary supplement ingredients have seen such a steep sales increase over the past five years as turmeric. Turmeric has been the top-selling dietary supplement in US natural food stores since 2013, and it ranked fifth in sales in mainstream retail outlets in 2017.

The earliest known reports of turmeric adulteration were published in the 1970s and 1980s and describe adulteration with other *Curcuma* species, starches, and dyes. More recently, the addition of undeclared synthetic curcumin or mixtures of synthetic curcuminoids to turmeric extracts has been reported. Curcumin is one of the naturally occuring curcuminoids found in turmeric root and rhizome. Synthetic curcuminoids can be produced for about one-third of the cost of natural curcuminoids, providing a financial incentive for fraudulent suppliers to dilute or replace turmeric extracts with synthetic materials.

The new bulletin, written by Ezra Bejar, PhD, an expert in botanical research, lists the known adulterants, details analytical approaches to detect adulterants, and provides information on the nomenclature, cultivation, harvest, and market importance of turmeric. It also discusses safety aspects of the known adulterants. Eighteen laboratory analytical experts from academia, government, and the herb industry provided input on the bulletin.

"The increased popularity of herbs like turmeric attracts producers and suppliers that are often more concerned about making a profit than they are about selling a high-quality botanical ingredient," said Mark Blumenthal, founder and executive director of ABC and director of BAPP. "While there are companies that produce and market high-quality, authentic, reliable turmeric powder and extract supplements, there are also adulterated turmeric ingredients on the market. The BAPP turmeric bulletin is designed to assist purchasing departments and quality control laboratories in the herb, spice, and dietary supplement industries in assuring that responsible companies purchase only authentic turmeric ingredients."

* An oleogum resin is a naturally occurring mixture of resin (a viscous mixture of terpenes), gum (a viscous exudate composed of polysaccharides), volatile oil, and small amounts of other substances.



ABC AHP NCNPR Botanical Adulterants Prevention Program

BOTANICAL ADULTERANTS BULLETIN

Turmeric (*Curcuma longa*) Root and Rhizome, and Root and Rhizome Extracts

By Ezra Bejar, PhD*

American Botanical Council, PO Box 144345, Austin, TX 78714

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Turmeric
Curcuma longa
Photo ©2018 Steven Foster

Keywords: *Curcuma longa*, turmeric, adulteration, turmeric root, turmeric rhizome, turmeric powder, curry, turmeric oleoresin, curcuminoids, curcumin

Goal: The goal of this bulletin is to provide information on issues of adulteration of turmeric (*Curcuma longa*) root, turmeric extracts, and curcuminoids, in particular with zedoary (*Curcuma zedoaria*, syn. *C. malabarica*), yellow colorants, and synthetic curcumin†. Also discussed is the mislabeling of previously extracted (spent) underground parts of turmeric as genuine turmeric root and rhizome. The bulletin may serve as guidance for quality control personnel, the international herbal products industry, and extended natural products community in general. It is also intended to present a summary of the scientific data and methods on the occurrence of species substitution, adulteration, the market situation, and economic and safety consequences for the consumer and the industry.

1. General Information

Common Names: Turmeric, common turmeric, Indian saffron#, yellow ginger[1-3]

1.2 Other Common Names:

Arabic: Kurkum[4]
Assamese: Lidar, halodhi[1,4,5]
Bengali: Halud[1,4,5]
Burmese: Tanum[1]
English: Curcuma[2,6]
Cambodian: Ro miet[7]
Chinese: Jiang huang (姜黄), [huang si] yu jin (郁金)[1,2,8,9 jianghuang,[10] yu chin[4]
Danish: Gurkemeje[10]
Dutch: Geelwortel[4]
Filipino (Tagalog): dilau, luyang-dilau[11]
French: Curcuma, safran des Indes[10]
German: Kurkuma, Gelbwurzel[10]
Gujurati: Haldar (હળદર)[1,4,5]
Hindi: Haldi, haldee (हल्दी)[12,13]
Italian: Curcuma, zafferano delle Indie, turmerico[4]
Japanese: Ukon[4]
Kannada: Arishina, arisina[1,4,5]
Laotian: Khi min[7]
Maley: Kooneit[1]
Malayalam: Manjal[1,4,5]
Marathi: Halad (हळद)[1,4,5]
Nepali: Besar (बेसार)[1,4,5,14]
Norwegian: Gurkmeie
Oriya: Haladi[1,4,5]
Portuguese: Açafrao-da-India[4]
Russian: Yellow ginger - zheltyj imbir' (жёлтый имбирь), curcuma (куркума)[4,14]
Spanish: Curcuma[4]
Sanskrit: Gauti, varnavat, haridra, marmadri, nisha, shati[4,10,13], haridra[13]
Swedish: Gurkmeja[1,4,5]
Tamil: Manjal[1,4,5]
Telegu: Pasupu, haridra[4]
Urdu: Haldi (ہلدی)[1,5,12]
Vietnamese: Nghệ, uất kim[7,14]

† Curcumin in this document is defined as the chemical compound diferuloylmethane, or (1*E*,6*E*)-1,7-bis(4-hydroxy-3-methoxyphenyl)hepta-1,6-diene-3,5-dione. The term curcumin is also used by members of the dietary supplement industry to describe a turmeric extract enriched in curcuminoids at a ratio of curcumin:demethoxycurmin:bisdemethoxycurcumin of approximately 77:17:3. To avoid confusion, extracts enriched in curcuminoids will be indicated as turmeric extracts.

The term "Indian saffron" is also used for saffron (*Crocus sativus*, Iridaceae) cultivated in India; the two materials should not be confused.

‡ The Chinese Pharmacopoeia lists the dry tuberous root of *C. longa*, *C. kwangsiensis*, *C. phaeocaulis*, and *C. wenyujin* as *yu jin*. *Curcuma longa* is specified as *huang si yu jin*.

Stefan Gafner, PhD, chief science officer of ABC and technical director of BAPP, added: "The use of colorants to make the turmeric root visually more attractive is of particular concern. Many of the yellow or orange colorants, such as lead chromate or metanil yellow, may represent a health risk. Since daily dosages of several grams of turmeric powder are recommended for health benefits, use of adulterated turmeric products may lead to an intake of excessive amounts of these colorants."

Boswellia Bulletin Describes Adulteration and Substitution with Resins from Related Species

Boswellia has been valued for its fragrance and medicinal properties for millennia. Retail sales of boswellia dietary supplements have skyrocketed in the United States, particularly in the mainstream channel, where sales increased from approximately $143,000 in 2013 to $14.6 million in 2017, corresponding to an average annual growth of roughly 210%.

Published data on boswellia adulteration have focused mainly on admixture or substitution with oleogum resins from other *Boswellia* species, in particular *B. frereana*, *B. papyrifera*, and *B. sacra*.

"*Boswellia serrata* is preferred in Western countries due to the number of clinical studies supporting its anti-inflammatory benefits," said Gafner. "In other areas of the world, substitution of *Boswellia serrata* with other *Boswellia* species may occur due to permissible interchangeable use. However, substitution or adulteration may also be due to shortages in the supply chain or the availability of material from other plants at lower cost." In addition, adulteration can occur due to misidentification of *B. serrata* along the supply chain.

The new bulletin was written by Allison McCutcheon, PhD, an expert in herbal medicine research in Vancouver, British Columbia. It summarizes the published data on boswellia quality issues (in particular the challenges in distinguishing *Boswellia serrata* from its potential substitutes and adulterants), details analytical methods to detect adulteration, and provides information on the nomenclature, cultivation, harvest, and market importance of boswellia. Twenty-two experts in quality control of medicinal plants from academia and the herb industry provided input on the bulletin.

According to Blumenthal: "The growing popularity of boswellia resin in dietary supplements and medicinal herb products that are designed to alleviate inflammatory conditions, coupled with credible reports of either substitution or dilution with undeclared lower-cost ingredients, prompted us to investigate and report on boswellia. The bulletin confirms that boswellia is subject to intentional adulteration by some suppliers, meaning that responsible buyers of boswellia raw material and extract need to exercise additional diligence in their quality control programs."



ABC AHP NCNPR
Botanical Adulterants Prevention Program

BOTANICAL ADULTERANTS BULLETIN

Boswellia serrata Adulteration

By Allison McCutcheon, PhD*

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Citation (JAMA style): McCutcheon A. Adulteration of *Boswellia serrata*. Austin, TX: Botanical Adulterants Prevention Program; Botanical Adulterants Bulletin. 2018.

Keywords: Adulterant, adulteration, *Boswellia*, *Boswellia serrata*, *Boswellia carteri*, *Boswellia frereana*, *Boswellia sacra*, *Boswellia papyrifera*, boswellic acids, *Garuga pinnata*, Indian frankincense, Pinaceae

Goal: The goal of this bulletin is to provide timely information and/or updates on issues of adulteration of *Boswellia serrata* (Burseraceae) to the international herbal industry and extended natural products community in general. It is intended to complement the previously published works with information on *B. serrata* adulteration by presenting new data on the occurrence of adulteration, the market situation, and consequences for the consumer and the industry.

1. General Information

1.1 Common name: Indian frankincense,[1] boswellia[2]

1.2 Other common names:

English: Indian olibanum[2,3]

Assamese: Sallaki[4]

Ayurvedic: Shallaki, susravaa, gajabhakshyaa, salai, gum-kunduru[5]

Bemba: Kundru[6]

Bengali: Luban, salai,[6] salgai[7]

Chinese: *Chi ye ru xiang shu* (齿叶乳香树)

French: Arbre à encens de l'Inde, boswellie, encens d'Inde[2]

Gujarati: Gugal, saleda, dhup,[6] shaledum, saladi, gugal, saledhi[4]

German: Indischer Weihrauch[2]

Hindi: Madi, salai, saler, salga, salhe, sali,[6] anduk, gugal, halar, kundur, loban, lobhan, luban, salaga, salai, salar, salaran, salhe, sel-gond, vellakkunturukkam,[7] labana[4]

Italian: Incenso indiano[8]

Kannada: Madimar, chilakdupa, tallaki, maddi[4]

Kashmiri: Kunturukkam, samprani[4]

Marathi: Salai cha dink[4]

Pharmacopoeial: Olibanum Indicum,[9] Gummi Boswellii[10]

Punjabi: Salaigonda[4]

Sanskrit: Sallaki, kunduru,[6] agavrttika, ashvamutri, asraphala, bahusrava, gajabhaksha, gajabhaksya, gajapriya, gajasana, gajashana, gajavallabha, gandhamula,

Boswellia serrata oleogum resin
Photo ©2018 Steven Foster

Boswellia serrata - Botanical Adulterants Bulletin • June *2018* • www.botanicaladulterants.org

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About the ABC-AHP-NCNPR Botanical Adulterants Prevention Program

The ABC-American Herbal Pharmacopoeia (AHP)-National Center for Natural Products Research (NCNPR) 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 members, researchers, health professionals, government agencies, the media, and the public about various challenges related to adulterated botanical ingredients sold in commerce. To date, more than 200 US and international parties have financially supported or otherwise endorsed the program.

The turmeric and boswellia bulletins are the 14th and 15th publications, respectively, in the series of Botanical Adulterants Bulletins. In total, BAPP has produced 42 peer-reviewed publications, including the Botanical Adulterants 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

American Herbal Pharmacopoeia Publishes Monograph and Therapeutic Compendium on Motherwort

On April 16, 2018, the American Herbal Pharmacopoeia (AHP) announced the publication of monograph standards and a therapeutic compendium for motherwort (*Leonurus cardiaca* and *L. quinquelobatus*, Lamiaceae) aerial parts. Motherwort aerial parts have been used in Asian healing traditions for approximately 2,500 years, with documented uses in the Western tradition dating back to the 15th century. The plant's common name refers to its widespread use as a childbirth aid and menopause aid, and for gynecological and reproductive issues. Clinical trials of motherwort also have investigated its potential therapeutic use in patients with hypertension, cardiac palpitations, and anxiety. The aerial parts of motherwort, a member of the mint family, can be prepared as a tisane, tincture, dry extract, or fluid extract, though they are most commonly sold as tisanes or tinctures.

The AHP monograph establishes authenticity, purity, and quality standards for raw materials and preparations. The therapeutic compendium provides a comprehensive review of pharmacological and safety data, including information on pharmacokinetics, pharmacodynamics, actions, medical indications, modern and traditional uses, structure and function claims, dosages, interactions, side effects, contraindications, toxicology, and more.

The publication is the result of a collaboration among AHP and researchers from the University Medical Center Göttingen in Germany; the Poznan University of Medical Sciences, Department of Pharmacognosy in Poland; the University of Medicine and Pharmacy Department of Pharmacognosy, Phytochemistry, and Phytotherapy in Bucharest, Romania; the University of Vienna in Austria; and the University of Reading in England. The publication's 12 authors and 19 reviewers are international experts from China, Kazakhstan, Uzbekistan, Russia, Austria, and the United States.



The macroscopic identification section of the monograph contains detailed, close-up, labeled photographs of fresh and dried motherwort aerial parts to aid field workers and others who handle raw materials. For comparison purposes, this section also includes photographs of Asian motherwort (*L. japonicus*), which is not accepted as an official motherwort species in Europe, the United States, or Russia. However, *L. japonicus* is listed in the official pharmacopeias of China, Germany, Japan, and Korea, which has resulted in some confusion in the international market. While these plants have very similar traditional uses, the monograph provides information about the methods to determine their morphological, chemical, and pharmacological differences.

The nomenclature and taxonomy discussion also notes that *L. quinquelobatus* was once considered a subspecies of *L. cardiaca* but is currently treated as its own separate species; this, however, is a recent taxonomic change that is not reflected in the American Herbal Products Association's *Herbs of Commerce*, 2nd edition. AHP President Roy Upton, the lead author of the monograph, takes great care to point out these taxonomic intricacies, and notes that *L. quinquelobatus* should not be considered an adulterant if it appears in a motherwort product.

In AHP's press release that announced the monograph and therapeutic compendium's publication, Upton was quoted as saying: "Motherwort is an underutilized botanical. Thanks to many international collaborators, this monograph represents the most complete body of information on motherwort to date."[1]

Motherwort is used mostly by traditional herbalists, particularly those with female clients. It has yet to appear, for example, in market data compiled by Chicago-based marketing firms SPINS and IRI as reported by the American Botanical Council (ABC) in its annual Herb Market Report. The report provides lists of the 40 top-selling botanicals in both the natural and mainstream market segments. However, with recent clinical studies investigating motherwort's potential antihypertensive and anxiolytic actions, the botanical could be poised for an increase in popularity among consumers.

AHP's monograph and therapeutic compendium provide information that can be used by a variety of individuals in the herbal community, from consumers and practitioners to quality control personnel and dietary supplement manufacturers.

ABC Chief Science Officer Stefan Gafner, PhD, praised AHP's extensive work on the monograph and therapeutic compendium and congratulated the organization for giving attention to a relatively unknown herb. "This is another extraordinary AHP monograph on an important medicinal herb that has not been considered by other standard-setting organizations," Gafner wrote (email, May 8, 2018). "The document covers the important aspects of the herb in detail, and it even has a separate section on the history of the plant at the end. I found the images and text for the macroscopic identification simply outstanding and believe that this part will be highly beneficial since the botanical material is still predominantly wildcrafted. Overall, this monograph will appeal to a broad audience, not only those who manufacture motherwort dietary supplements, but also those who use it in their medical practice."

The monograph is available for purchase through the AHP website.[2] HG

—Hannah Bauman

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Motherwort
Leonurus cardiaca
Photo ©2018 Steven Foster

Clinical Efficacy of a Chinese Herbal Combination for Mild Cognitive Impairment

Reviewed: Tian J, Shi J, Li T, et al. Efficacy and safety of an herbal therapy in patients with amnestic mild cognitive impairment: A 24-week randomized phase III trial. *Evid Based Complement Alternat Med.* 2017;2017:4251747. doi: 10.1155/2017/4251747.

Study Details: At a Glance	
Participants	• 324 men and women • Diagnosed mild cognitive impairment • 55-80 years of age
Study Design	Randomized, double-blind, placebo-controlled phase III study
Study Length	24 weeks
Active Treatment	Multi-herb formula ("shenwu capsule"; North China Pharmaceutical Group Corporation [NCPGC]; Hebei Province, China) plus placebo
Comparative Treatment	Donepezil (Aricept; Eisai Inc.; Tokyo, Japan) plus placebo
Disclosures	The study was sponsored by NCPGC. Three of the authors (Z. Wang, X. Li, and Z. Lv) are employees of NCPGC, and one author (Q. Zheng) received grants from NCPGC for data collection and biostatistical analysis.

Mild cognitive impairment (MCI) refers to a stage of cognitive impairment between what is expected with normal aging and the onset of Alzheimer's disease (AD). Amnestic MCI (aMCI) is the most common subtype of MCI and is characterized by impairment of episodic memory without impairment of activities of daily living (ADL). Treating aMCI may prevent or delay the onset of AD. The purpose of this multicenter, randomized, double-blind, double-placebo, parallel-controlled, phase III study was to evaluate the efficacy and safety of a Chinese herbal formulation to improve cognition and memory in patients with aMCI.

Chinese-speaking adults (N = 324; 55-80 years of age) with MCI who were living in the community (as opposed to senior care facilities) were recruited from nine memory clinics in China from September 2008 to May 2010.

Included patients had memory complaints that were corroborated by an informant; abnormal memory function according to the Chinese version of the Adult Memory and Information Processing Battery (AMIPB) Logical Memory Delayed Story Recall (DSR) subtest; normal general cognition based on the Mini-Mental State Examination (MMSE); no or minimal impairments in ADL; scores of 12 or less on the Hamilton Depression Rating Scale (HAM-D) and 4 or less on the Hachinski Ischemic Score (HIS) scale; adequate vision and hearing; and no or mild medial temporal atrophy or hippocampal volume atrophy on a magnetic resonance imaging (MRI) scan. In addition, included patients were not significantly impaired cognitively or functionally according to the National Institute of Neurological Disorders and Stroke and Alzheimer's Disease and Related Disorders Association criteria for AD and met the criteria for stage 2-3 on the Global Deterioration Scale (GDS).



Asian Ginseng
Panax ginseng
Photo ©2018 Steven Foster

Patients were excluded if they had evidence of a focal brain lesion; a previous head injury with loss of consciousness or immediate confusion after the injury; a neurologic disease that might affect cognition; uncontrolled hypertension or diabetes mellitus; a history of significant cerebrovascular disease, a central nervous system infarct or infection, a major psychiatric disorder, or alcohol or substance abuse. Patients also were excluded if they had documented evidence of an active gastric or duodenal ulcer within the previous three months; active malignancy or prostate cancer within the preceding 24 months; or chronic or acute renal, hepatic, or metabolic disorder; among other criteria.

Following a two-week placebo run-in phase, patients had an MRI scan and then were randomly assigned to receive for 24 weeks either an herbal capsule (five capsules three times per day) and a placebo that was identical to donepezil tablets (Aricept; Eisai Inc.; Tokyo, Japan) (n = 216), or 5 mg per day donepezil and a placebo that was identical to the herbal capsules (n = 108).

The herbal capsule (shenwu capsule; North China Pharmaceutical Group Corporation; Hebei Province, China) contained 4.24% Asian ginseng (*Panax ginseng*, Araliaceae) root, 21.28% *he shou wu* (*Polygonum multiflorum*, Polygonaceae) tuber, 14.89% epimedium (*Epimedium brevicornum*, Berberidaceae) leaf, 14.89% *Acorus tatarinowii* (Acoraceae) rhizome, 14.90% Sichuan

lovage (*Ligusticum sinense*, Apiaceae) rhizome, and 29.80% lobed kudzu vine (*Pueraria* spp., Fabaceae) root extracts.


Polygonum multiflorum
Photo ©2018 Steven Foster

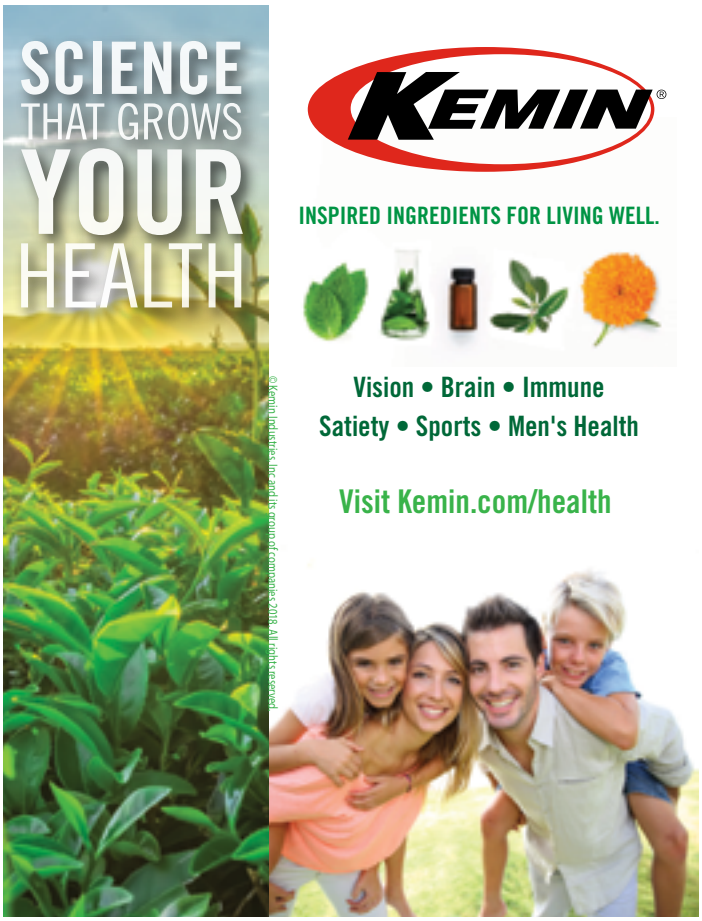
Cognition was the primary outcome assessed using the Alzheimer's Disease Assessment Scale-cognitive subscale (ADAS-cog). The secondary outcomes measured memory with the DSR logical memory subtest. Assessments were made at screening and weeks 12 and 24. An additional evaluation was carried out at week 48, although with a limited number of participants (n = 23). The safety assessment included examinations of general physical vital signs (e.g., breathing, heart rate, and blood pressure), electrocardiography (ECG), laboratory testing, and documentation of adverse events (AEs).

A total of 44 patients discontinued treatment, with two patients in the herbal therapy group discontinuing due to AEs. Baseline demographics and characteristics (including MMSE, GDS, and HAM-D scores) were not significantly different between groups. Both groups had excellent compliance (herbal therapy: 92.6% and donepezil: 95.3%). ADAS-cog and DSR scores were significantly improved from baseline to week 24 in both treatment groups ($P < .001$), and there were no significant between-group differences in these scores at 24 weeks. The inferiority analysis showed that the herbal treatment was not inferior to donepezil. The herbal therapy produced an average 4.19-point improvement in ADAS-cog scores from baseline to week 24 (an improvement of at least 3.3 points is considered clinically significant). At week 48 (24 weeks after the treatment period ended), scores for both groups trended toward original baseline values. The rate of conversion from MCI to AD in 23 subjects (11 patients from the herbal therapy group and 12 patients from the donepezil group) was assessed at one site. At week 24, none of the patients converted to AD in either group.

AEs were reported by 18.1% of the herbal therapy group and 57.4% of the donepezil group. The most frequent AEs assessed as probably related to the herbal therapy were thirst (6.5%) and sore throat (4.2%). The herbal therapy group compared to the donepezil group had significantly lower rates of diarrhea (0% vs. 12.5%, respectively), nausea (2.1% vs. 16.7%), and insomnia or abnormal dreams (2.3% vs. 16.7%) ($P < .05$ for all). There were no significant changes in vital signs, physical examination findings, ECG status, or laboratory values.

The authors concluded that the herbal therapy was safe and has similar clinical benefits to donepezil with fewer AEs in patients with confirmed MCI. A limitation of the study is that there was no true placebo group. Although there was a positive control (donepezil), all patients knew that they were being treated with one of two active preparations, so a placebo response cannot be ruled out. Another limitation is that 24 weeks may not be long enough to see a long-term response in patients with MCI. Additional research is needed to identify the key bioactive constituents of these plants that may be responsible for the observed effects and confirm whether the herbal therapy delays the progression from MCI to dementia. HG

— Heather S. Oliff, PhD



Review of a Proprietary Hawthorn Extract for Treating Heart Failure

Reviewed: Holubarsch CJF, Colucci WS, Eha J. Benefit-risk assessment of *Crataegus* extract WS 1442: an evidence-based review. *Am J Cardiovasc Drugs*. 2018;18(1):25-36.

Study Details: At a Glance	
Participants	Various
Study Design	Literature review and risk-benefit assessment
Study Length	Various
Active Treatment	Dry extract of hawthorn flowers and leaves (WS 1442; Dr. Willmar Schwabe GmbH & Co. KG; Karlsruhe, Germany)
Control	Various
Disclosures	All of the authors received honoraria from Schwabe for conducting and writing the SPICE study.

The leaves and flowers of hawthorn (*Crataegus laevigata* and *C. monogyna*, Rosaceae) have been used to treat heart ailments for more than 2,000 years. Based on the cumulative scientific evidence, the German Commission E issued positive monographs for hawthorn berry and leaf with flower preparations to treat decreasing functional capacity of the heart,[1] and in 2016, the European Medicines Agency's Committee on Herbal Medicinal Products recognized hawthorn as a "traditional herbal medicinal product used to relieve symptoms of temporary nervous cardiac complaints."[2]

One of the most extensively studied hawthorn preparations is the proprietary extract WS 1442 (Dr. Willmar Schwabe GmbH & Co. KG; Karlsruhe, Germany). WS 1442 is a dry extract of hawthorn flowers and leaves (drug extract ratio of 4-6.6:1; extraction solvent 45% ethanol) containing 17.3% to 20.1% oligomeric procyanidins, as well as flavonoids, triterpenoids, and phenol carboxylic acids.

This review and risk-benefit analysis focused on the safety and efficacy of WS 1442 in the treatment of patients with New York Heart Association (NYHA) class II or class III heart failure, and included sub-analyses of the effects of WS 1442 on patients with systolic heart failure (heart failure with reduced ejection fraction [HFrEF]) and diastolic heart failure (heart failure with preserved ejection fraction [HFpEF]).

An overview of 24 preclinical studies of WS 1442 is provided. The results of the studies support WS 1442's ability to provide positive inotropic properties (strengthening the force of heart contractions) and antiarrhythmic properties; myocardial protection from ischemic damage (damage caused by restricted blood supply to tissue), reperfusion injury (injury caused by return of blood supply to tissue), and hypertension-related hypertrophy; improved endothelial functions such as nitric oxide synthesis; and delayed endothelial senescence (age-related deterioration of the endothelium).

Safety Review

A 2006 systematic review of hawthorn safety identified 14 studies of WS 1442, including 10 randomized controlled trials (RCTs), two uncontrolled trials, one observational study, and one cohort study. A cumulative total of 1,563 subjects (n = 395 in controlled trials and n = 1,168 in uncontrolled studies) consumed WS 1442 at doses up to 1,800 mg per day for up to 16 weeks. One trial included healthy subjects, while the remainder recruited patients with NYHA class I-II or II-III heart failure. In the RCTs, the incidence of adverse effects (AEs) did not significantly differ between the WS 1442 and control groups. No causal relationship was found between WS 1442 dose and AEs, and no AE potentially related to WS 1442 was considered serious.

In the 2008 placebo-controlled, double-blind, multicenter SPICE (Survival and Prognosis: Investigation of *Crataegus* Extract WS 1442 in Congestive Heart Failure) trial, 2,681 adults with NYHA class II or III congestive heart failure and reduced left ventricular ejection fraction (LVEF) received 900 mg daily of WS 1442 or placebo for 24 months as an adjunct to standard cardiac medications. About 90% of the participants took at least three conventional cardioactive drugs. The incidence of serious AEs was 39.2% in the WS 1442 group and 41.1% in the placebo group, with similar types of AEs reported in both groups. No specific AEs related to WS 1442 were observed.

In the 2009 Hawthorn Extract Randomized Blinded Chronic Heart Failure (HERB CHF) trial (N = 120), WS 1442 or placebo was given to patients with NYHA class II-III chronic heart failure to investigate the effect of WS 1442 on submaximal exercise capacity. AEs were experienced by 60% of patients in the WS 1442 group and by 38.3% in the placebo group. Twelve patients in each group reported cardiac-related AEs. The incidence of cardiac AEs and common AEs was comparable between groups. The investigators concluded that it was unlikely that the wide variety of AEs in the hawthorn group may be "explainable by a pharmacological effect of WS 1442 and may have been attributable to chance."

No suspected AEs or drug interactions attributed to hawthorn have been reported to health authorities, and no possible drug interactions with WS 1442 were observed in the reviewed trials.

Efficacy Data

Heart failure treatments aim to reduce morbidity and hospitalization and improve symptoms and quality of life (QoL). In the SPICE trial, the cumulative first cardiac event

rates were lower in the WS 1442 group compared with the placebo group, although the difference between groups was not statistically significant. However, WS 1442 patients with baseline LVEF values at the upper limit for inclusion in the study (25-35%) had a significantly lower cumulative risk for cardiac mortality and sudden cardiac death compared to the placebo group. "The results point to a potential antiarrhythmic and/or anti-ischemic effect already observed in animal models," wrote the authors.

The 2008 Cochrane review of hawthorn included 11 RCTs that evaluated the effect of WS 1442 on heart failure symptoms and QoL. Meta-analysis of the two WS 1442 trials that evaluated exercise tolerance indicated that exercise tolerance was significantly increased from baseline in the WS 1442 group ($P < 0.001$). The pressure-heart rate product, an index of cardiac oxygen consumption, was assessed in five of the included WS 1442 trials, and meta-analysis of the results showed that the pressure-heart rate product was significantly reduced in WS 1442 patients compared to placebo ($P = 0.01$), indicating a significant increase in cardiac performance in patients treated with WS 1442.

Two studies in patients with HFrEF found that WS 1442 significantly reduced LVEF compared to placebo ($P < 0.01$ and $P = 0.04$, respectively). In the two studies that evaluated the time to accomplish a specified walking distance, one found that WS 1442 significantly reduced the time in patients with HFpEF ($P = 0.02$), while the other found that WS 1442 had no significant effect in patients with HFrEF. Three studies evaluated the effect of WS 1442 treatment on QoL — one found no significant difference between WS 1442 and placebo; one reported a trend toward significance with WS 1442; and one found WS 1442 significantly improved QoL in patients with HFpEF.

Risk-Benefit Assessment

Based on the extant clinical evidence, hawthorn preparations appear to cause few, mainly transient, and non-serious AEs. For WS 1442 in particular, there have been no serious AEs and no indications of possible drug interactions in large-scale, long-term studies. "It is therefore concluded that *Crataegus* extract WS 1442 has a very favorable safety profile even when administered as a part of a polydrug regimen," the authors wrote. In terms of efficacy, evidence from RCTs indicates that WS 1442 can improve cardiac performance and exercise tolerance, ameliorate heart failure symptoms, and improve cardiovascular health-related QoL. The authors also noted that the risk-benefit assessment for WS 1442 in the treatment of patients with NYHA class II or III heart failure is positive.

The authors concluded that WS 1442 is a safe herbal medicinal product that can improve functional capacity, symptom control, and cardiovascular health-related QoL in patients with HFrEF and HFpEF. They acknowledged that a limitation of this review "is that some of the evidence ... originated from older, comparatively small, and partly uncontrolled research, so confirmation by controlled trials meeting current rigorous scientific standards would be highly welcome." HG

—Shari Henson

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Hawthorn
Crataegus laevigata
Photo ©2018 Steven Foster

Systematic Review of Kratom: Risks and Benefits for Mental Health

Reviewed: Swogger MT, Walsh Z. Kratom use and mental health: a systematic review. *Drug Alcohol Depend.* 2018;183:134-140.

Study Details: At a Glance	
Study Design	Systematic review
Included Studies	13 cross-sectional or retrospective studies
Study Length	N/A
Active Treatment	N/A
Control	N/A
Disclosures	The authors declared no conflicts of interest or outside funding sources.

In this systematic review of the scant literature on the effects of kratom (*Mitragyna speciosa*, Rubiaceae) leaf on mental health, authors Marc Swogger, PhD, and Zach Walsh, PhD, contend that the 2016 public warnings by the US Centers for Disease Control and Prevention (CDC) and Drug Enforcement Administration (DEA) of possible kratom-induced psychosis or death are unsupported by evidence. The authors are clinical psychologists with a strong record of research and publications on the behavioral and mental health effects of psychoactive substances. According to the authors, criminalizing kratom would increase potential harms, restrict research, and deny access to possible benefits. Reminiscent of the 1930s criminalization of "marihuana" (cannabis [*Cannabis* spp., Cannabaceae]), the authors believe that some government statements and media stories have fomented "drug hysteria" regarding kratom.

Kratom leaves have been used for centuries in Southeast Asia for pain, cough, and diarrhea; enhanced energy and stamina; and as an opioid substitute or to relieve opioid withdrawal symptoms. Traditionally chewed fresh or taken in a water infusion, leaves may also be smoked or vaporized. Kratom products (e.g., extracts, capsules, gums, and powders) are widely available in North America and Europe, and via the internet. Processed, concentrated products raise new concerns about potential adverse effects (AEs), making kratom research particularly timely.

Many of kratom's potential risks and benefits are in the realm of mental health. The authors searched for reports that were published between January 1960 and February 2017.* Case studies were excluded, as were studies with inadequately described methods. Of 49 initial results, after excluding duplicates and those that did not meet criteria, 13 cross-sectional or retrospective studies were reviewed. Nine reported on user surveys in Thailand or Malaysia; two on calls to US poison control centers; and two on US surveys on kratom use. The presented results pertain to harm reduction, mood, and AEs.

In the United States, misuse of prescribed and prohibited opioids has reached "catastrophic" levels, according to the authors. They state that new approaches to opioid harm reduction and cessation are needed. Harm from drug abuse can be reduced, for example, by substituting substances with similar effects but that cause less severe harm (e.g., methadone or buprenorphine use for opioid

* It is unclear if the authors searched for reports on kratom alone or included its alkaloids mitragynine and 7-hydroxymitragynine, which are unmentioned in their review.

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addiction). Two Malaysian studies suggest that kratom may have potential in opioid substitution. In one study of 136 users, most of whom were men who reported low education and/or a history of drug use, 90% used kratom as an opioid substitute, and 84% said it helped with withdrawal symptoms. In the other study of 293 men, who were generally younger (mean age = 28) and better educated (66% reported at least an upper secondary education) than those in the first study, 15% used kratom to reduce or stop use of "illicit substances" (e.g., opioids, cannabis) and/or manage withdrawal. Of 8,049 respondents to a US-based internet survey, almost half said they used kratom to reduce or stop opioid use. A minimum dose of 5 g was deemed effective by these respondents. Nearly half were women, a population traditionally underrepresented in kratom research, and 80% reported some college education. This study also reported on the use of kratom for mood effects. Respondents who had Medicare, Medicaid, no insurance, or were self-insured were more likely to use kratom for its mood-enhancing and opioid-substituting effects. Female gender and being married were negatively associated with both uses.

Kratom is reported as energizing at low doses and calming at higher ones. In one of the Malaysian studies cited above, 28% of 293 male users said that kratom boosted energy and alertness, and 26% said that it brought about euphoria, relaxation, or contentment. Of 161 kratom users who responded to a US-based survey, 30% reported an enhanced sense of well-being and 9% reported increased energy. Kratom users often mention its relaxing and anxiety-reducing effects, but none of the reviewed studies specifically addressed kratom's anxiolytic effects, especially relative to sedation or impaired social motivation, which are drawbacks to some common anxiolytics. Drowsiness and sedation were reported by 19.4% of 660 people who called US poison control centers after taking kratom (2010-2015). However, more than 40% of those who reported drowsiness and sedation had used other substances concurrently. Of the 8,049 respondents in the large US-based survey mentioned previously, 79.4% reported more energy, 75.6% reported less depressed mood, and 74.3% reported less anxiety. Energizing effects were reported with intake of 1 g or less; benefits to depression and anxiety were reported with intake up to 5 g.

Psychosocial AEs of kratom use typically are related to tolerance, withdrawal, and difficulty in abstaining. In ethnically and culturally diverse studies, reported withdrawal symptoms include fatigue, craving, tremors, muscle cramps/aches, insomnia, anxiety/tension, depressed mood, nausea/vomiting, hot flashes/sweating, diarrhea, and watery eyes. These symptoms resemble symptoms of opioid withdrawal but lack comparable intensity or duration. There is no evidence that kratom causes psychopathology or aggression. While 4% of subjects in a Malaysian study who were asked specifically about hallucinations had experienced such visual anomalies, these may have been caused by other substances ingested, existing psychopathology, or respondents confusing "hallucinations" with a mild visual perception enhancement, which has been reported as a kratom effect. The authors conclude that "kratom use appears to have several important mental health benefits that warrant further study. Kratom dependence is a risk for some people, though the dependence syndrome appears to be mild in its psychosocial and physiological effects relative to that of opioids." HG

—Mariann Garner-Wizard



Kratom
Mitragyna speciosa
Photo ©2018 Uomo Vitruviano

Review Finds Substantial Evidence Supporting Some Medicinal Benefits of Cannabis and Cannabinoids

Reviewed: Grotenhermen F, Müller-Vahl K. Medicinal uses of marijuana and cannabinoids. *CRC Crit Rev Plant Sci*. 2016;35(5-6):378-405. doi: 10.1080/07352689.2016.1265360.

In a special double issue on cannabis (*Cannabis* spp., Cannabaceae) in *Critical Reviews in Plant Sciences*, authors Franjo Grotenhermen, MD, and Kirsten Müller-Vahl, MD, review the evidence for the medicinal uses of cannabis- and cannabinoid-based medicines reported in clinical studies from 1975 to 2015.

Study Details: At a Glance	
Study Design	Literature review
Included Studies	140 controlled clinical trials published from 1975 to 2015
Study Length	Various
Active Treatment	Various cannabis- or cannabinoid-based preparations
Control	Various
Disclosures	None declared

History of Medicinal Cannabis

In the introduction, the authors note that cannabis has been used as a medicine for centuries in cultures around the world. The therapeutic use of cannabis was first well-described in Europe in 1830 by Theodor Friedrich Ludwig Nees von Esenbeck, a professor of botany and pharmacy at the University of Bonn in Germany. The better-known Sir William Brooke O'Shaughnessy, an Irish physician, described medicinal uses of cannabis in an account that appeared nine years later. Following those reports, cannabis tinctures became popular in the West and were manufactured by pharmaceutical companies in Germany, the United Kingdom, and the United States.

However, by the beginning of the 20th century, the medicinal use of cannabis preparations was in steep decline. Glossing over the United States' prohibition of cannabis that began in the late 1930s, the authors suggest that cannabis' simultaneous medicinal decline was a result of the late elucidation of its unique active constituents, the cannabinoids, which began to be understood only in the 1930s and 1940s. In contrast, the authors note, many other plant constituents had been identified by the late 1800s. The authors speculate that if cannabinoids been identified and separated earlier, then standardized preparations would have been available and, by the second half of the 20th century, synthesized for use in approved medicines.

Research and Regulation

Despite increasing evidence for therapeutic benefits of cannabis and cannabinoids in many conditions, "healthcare authorities in most countries handle cannabis and single cannabinoids as newly detected medicinal drugs," each of which must "undergo rigid and expensive approval procedures comparable to entirely new molecules." This "cannabis dilemma," as the authors describe it, is compounded because many of these compounds have uniquely broad therapeutic applications, unlike most modern single-entity pharmaceutical agents.

Reliable evidence from large randomized controlled trials (RCTs) of cannabis preparations is available for only a few indications. Lawmakers and physicians increasingly acknowledge, however, that "seriously ill and otherwise treatment-resistant patients cannot be deprived from effective therapy," even if such a therapy is not officially approved.

The discovery that the effects of tetrahydrocannabinol (THC), the principal psychoactive constituent of cannabis, are mediated by specific binding sites, including cannabinoid receptor type 1 (CB_1) and cannabinoid receptor type 2 (CB_2), was first demonstrated in 1988.[1] It is interesting to speculate how cannabis might have been regulated if the endocannabinoid system (ECS) and its endogenous cannabinoids (endocannabinoids) had been known in the 1940s or before. At the time of this report, more than 200 endocannabinoids and endocannabinoid-like substances have been identified, along with evidence of their widespread effects on many physiological systems.

In the cannabis plant, 120 cannabinoids have been identified. Most of cannabis' known effects are based on THC's agonistic actions at CB_1 and CB_2 sites; however, THC also acts on other receptor systems. After THC, cannabidiol (CBD) is the next most-studied cannabinoid, with antagonistic effects at CB_1, agonistic effects at vanilloid receptors type 1 (VR_1) and type 2 (VR_2), and binding at other receptor sites.

Review of Controlled Clinical Trials

The article summarizes 140 controlled clinical studies (N = approx. 8,000) in tables organized by indication. The following cannabis preparations were used in these trials:

- Smoked or vaporized cannabis herbal material ("marijuana");
- Sativex oromucosal spray (nabiximols; standardized extract of cannabis flower and leaf with a 1:1 ratio of THC and CBD; GW Pharmaceuticals; Cambridge, United Kingdom), approved in several countries to treat spasticity in multiple sclerosis (MS);
- Dronabinol (sold under various brand names, including Marinol; AbbVie Inc.; Chicago, Illinois), a form of synthetic THC that is licensed in the United States for cancer-related nausea and vomiting and HIV/AIDS-related loss of appetite;

- Nabilone (Cesamet; Valeant Pharmaceuticals; Costa Mesa, California), a synthetic cannabinoid similar to THC that is approved in the United Kingdom, United States, and Canada for side effects of cancer chemotherapy;
- CBD, approved in some US states for epilepsy and other indications.* For example, in Iowa, qualifying conditions for CBD use include HIV/AIDS; amyotrophic lateral sclerosis (ALS); cancer; cancer-related chronic pain, nausea, or cachexia (weakening or wasting of the body in chronic illness); Crohn's disease; MS; Parkinson's disease; intractable epilepsy; terminal illness; and untreatable pain; and
- A few other single cannabinoids.



Cannabis
Cannabis sativa
Photo ©2018 Matthew Magruder

For chemotherapy-induced nausea and vomiting, 33 trials (including 30 RCTs) with a total of 1,525 patients reported that nausea and vomiting were reduced with THC preparations or Sativex; the latter added benefit to standard antiemetic therapy when used concurrently. For appetite loss and cachexia in patients with cancer or HIV/AIDS, 10 controlled studies (including seven RCTs) with a total of 973 patients reported significant benefits to taste and smell perception, appetite, caloric intake, quality of sleep, and quality of life with THC supplementation or smoked cannabis. In 35 controlled trials (including 18 RCTs) with a total of 2,046 patients with neuropathic or chronic pain, Sativex resulted in improvements in pain and sleep quality, and both low-THC and high-THC cannabis delivered by vaporizer effectively reduced central or peripheral neuropathy in patients resistant to other analgesics. The efficacy and safety of both Sativex and smoked cannabis for spasticity from MS have been well-demonstrated in 14 controlled trials with a total of 1,740 patients.

Not all results of studied cannabis medicines are positive. In 11 controlled studies (including seven RCTs) on experimental[2†] or acute pain, with 377 total patients, neither THC, Cannador (a discontinued standardized extract in pill form with a 2:1 ratio of THC to CBD), nor nabilone showed significant benefits. However, one trial found a synergistic interaction between THC and morphine,[3] and another RCT of intramuscular levonantradol (a synthetic analog of THC) showed pain-reduction benefits.[4] In two of three studies of cannabis extract or smoked cannabis, reductions in pain were seen at low doses,[5,6] though high doses increased pain in one study.[7]

Other controlled studies of cannabinoids have been performed for conditions including tremor and bladder dysfunction in MS, spinal cord injury, Tourette's syndrome, glaucoma, dystonia, irritable bowel syndrome, Crohn's

* States with CBD-specific "medical marijuana" laws have not passed medical cannabis laws that would allow use of cannabis herbal material or any unapproved cannabinoids.

† Experimental pain tests included heat, cold, pressure, and single and repeated transcutaneous electrical stimulation.



disease, pulmonary disease, schizophrenia, and Parkinson's disease. For almost all, the limited evidence is favorable. Three studies using CBD[8-10] and one using nabilone[11] demonstrated improvements in patients with post-traumatic stress disorder and anxiety. Only one small RCT has investigated CBD in generalized epilepsy uncontrolled by standard medications.[12] Of eight patients receiving CBD for as long as four-and-a-half months, four were almost convulsion-free during the study and three more showed clinical improvements.

For most indications, only small, uncontrolled studies and/or case reports are available. Among these, notable benefits were seen in an open-label clinical study of women with trichotillomania (compulsive hair-pulling) treated with dronabinol.[13]

A few controlled studies have examined potential adverse effects of cannabinoids and their interactions with some drugs. THC is metabolized mainly in the liver by cytochrome P450 (CYP) isoenzymes (especially CYP2C), and it may interact with other substances metabolized by the same path. Smoking cannabis also can reduce plasma levels of some antipsychotic drugs. However, in studies of patients with cancer and HIV/AIDS, levels of cytostatic or antiretroviral drugs metabolized by CYP2C were not altered by concurrent THC treatment. The additive effect of THC taken with many analgesics and antiemetics is generally a desirable interaction. However, when taken with substances such as amphetamines that act on the cardiovascular system, the additive effects may increase tiredness. CBD helps to slow the degradation of some proton pump inhibitor drugs, as well as clobazam and risperidone (used for epilepsy and psychosis, respectively).

Many traditional and folk indications for cannabis have not been studied in controlled clinical trials. Uses for rheumatism, tetanus, rabies, and delirium tremens described by O'Shaughnessy, for example, have not been clinically investigated. Uses for joint inflammation, migraine, muscle cramps, and asthma, which were commonly treated by cannabis products in the 19th century and even after "marihuana" prohibition took effect in the 1930s, also have not been studied. Evidence from RCTs suggests that cannabis can improve sleep parameters in several conditions that may disrupt sleep, but its specific use in sleep disorders is unstudied. Other widespread but unstudied traditional uses for cannabis are for depression; alcohol, opioid, and/or nicotine withdrawal; premenstrual syndrome; women's reproductive health; and childbirth.

The authors note that pharmaceutical companies are working to develop synthetic compounds that modulate the ECS. As laws that "inhibit access to potential natural remedies for serious diseases" are repealed, cannabinoids may help physicians and patients find new ways to manage disease. HG

—Mariann Garner-Wizard

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Herbal Legacy Company: Thayers Natural Remedies

By Karen Raterman

Editor's note: This is the third article in our series of profiles on herb companies that have been operating for more than 100 years.

The year was 1847, and Henry Thayer was 19 years old when he founded Henry Thayer & Company in Cambridge, Massachusetts, and began selling his natural elixirs exclusively to medical professionals. More than 170 years later, the company, now known as Thayers Natural Remedies, is still a thriving provider of natural personal care products that carry the founder's name and bear his picture. Today, these products are sold in natural and specialty retail stores as well as in mainstream retail outlets in the United States and internationally. The company has stayed relevant by sticking to its roots and Henry Thayer's vision of relying on the power of nature to protect, soothe, and revitalize the body.

Henry Thayer was trained early in the medical arts.[1] The son of a physician from one of Massachusetts' founding families, he drew on that background and knowledge to launch his laboratory and apothecary on Main Street in Cambridge, where he produced herbal tinctures, infusions, syrups, and salves. Prominent among his products was Witch Hazel Extract, which was described as a "tonic, astringent and sedative."

Over time, Thayer expanded his line to include more than 800 products, such as infusions, poultices, syrups, tinctures, and wines. By 1861, Henry Thayer & Company was considered the largest pharmaceutical company in the United States, according to company literature.[1]

The early success of Thayer's products may be attributed to the fact that the young physician was ahead of his time in thinking about illnesses and medical treatments. Years earlier, during the Colonial period, many medical practitioners still attributed health problems to an imbalance of humors, or bodily fluids (namely, blood, phlegm, black bile, and yellow bile) — a medical theory that dates back to ancient Greece. An imbalance was "corrected" by bleeding, purging, and sweating and then replenishing the fluids with rest, diet, and medicinals (a practice referred to as "heroic medicine" in medical histories).[2]

By the mid-19th century, however, theories were beginning to change, and Thayer was among the pioneers of a more modern medical practice. Thayer was one of the first in the United States to create and sell natural, safe, and effective commercial remedies to address common ailments like colds, allergies, and sore throats.[1]

Thayer also was influenced by medicinal treatments used by the indigenous peoples of New England.[1] Witch hazel (*Hamamelis virginiana*, Hamamelidaceae), for example, can be found along damp stream banks in wooded areas of the region. Thayer noticed that Native American tribes grew, extracted, and applied witch hazel to their skin to reduce inflammation and heal cuts. Native tribes around Cambridge also sucked on the fibrous, red inner bark of slippery elm (*Ulmus rubra* syn *U. fulva*, Ulmaceae) to soothe sore throats.

The company was recognized early in its history for achievements in product development and manufacturing. In 1855, the American Institute of New York awarded Thayers a silver medal for excellence in preparation of fluid extracts. In 1856, the Massachusetts Charitable Mechanics Association recognized the company for the apparatus it used to produce these extracts.[3]

While Henry Thayer died in 1902, the company believes that its simple, steadfast premise has endured: to make products with simple, pure botanical ingredients that clean and nourish skin naturally. That same year, the company launched its slippery elm lozenges, which remains one if its oldest products.



Illustration of Henry Thayer, MD
Image courtesy of Thayers.

The efficacy of these individual formulas is one reason for Thayers' staying power, according to John Reppucci, vice president of sales and marketing at Thayers. "These medicines have stood the test of time," he said (email, March 13, 2018). "These natural elixirs have been a fixture in medicine cabinets for generations. Through a long-standing commitment to create pure, effective, cruelty-free products of the highest natural quality, [Thayers] has built a loyal consumer base. In fact, according to SPINS data, Thayers is the number one witch hazel brand in the natural channel, a position it has held for [more than] five years, and the number one slippery elm lozenge brand."



Historic bottle of Bay Rum product.
Image courtesy of Thayers.

For many people, these products also have a lasting and personal legacy. For example, in a recent interview in the company's newsletter titled "1847," Marlene Adelmann, founder and director of the Herbal Academy, an international school of herbal arts and sciences in Bedford, Massachusetts, noted that she remembers seeing Thayers Witch Hazel on both her grandmother and mother's dressing tables. Although Adelmann said she makes many of her own herbal beauty products, Thayers Witch Hazel is one store-bought exception. "I can't remember a time when this bottle was not on my bathroom shelf."[4]

Time-Tested Ingredients

A critical reason that Thayers' products have remained relevant is that the company, now based in Easton, Connecticut, has worked to balance its mission to develop natural products and treatments while also making them work well for today's consumers. "Though the company is no longer Thayer-family owned, it remains a family-owned company that emphasizes the importance of remaining faithful to our core mission and values," said Reppucci (email, April 6, 2018).

While the company's operations have evolved over the past two centuries, the ingredients the company uses have stayed relatively unchanged. The main difference between the products Thayers produces today and those first made by Henry Thayer in 1847 are the finished forms in which the ingredients are used, Reppucci noted. The current line of lotions, sprays, mists, and gels are much easier to use than the original methods of rubbing bark on the body or throat. Today, the ingredients are combined with other ingredients, such as oatmeal (*Avena sativa*, Poaceae), menthol (derived from various *Mentha* [Lamiaceae] species), and camphor (derived from the camphor laurel [*Cinnamomum camphora*, Lauraceae]), to help bring these natural remedies to modern consumers, he explained.

The company now produces products featuring its signature ingredients in three basic categories: skin care products (facial toners and astringents), health care remedies (lozenges, saline sprays, and joint support remedies), and dry mouth products (sprays and lozenges).

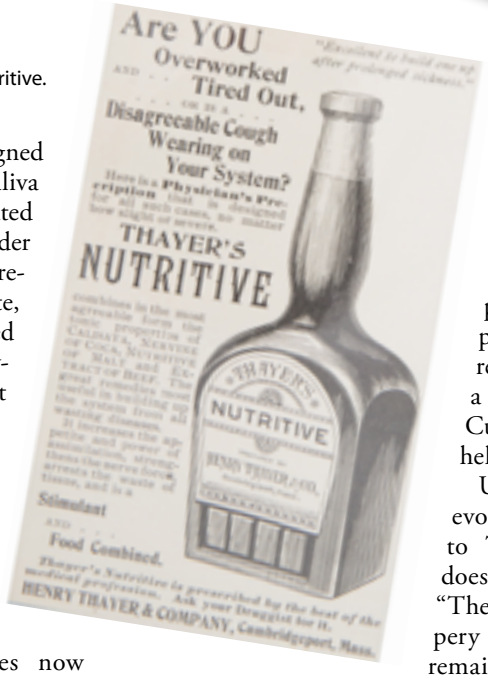
The brand's flagship ingredient, witch hazel, is a flowering tree with toothed, egg-shaped leaves and small, yellow flowers. It is known for its medicinal properties and was the basis for Henry Thayer's first product. Traditionally, witch hazel leaf and bark extracts have been used externally as a liniment for inflammation and bruises.[5] Witch hazel extract is commonly used in alcohol-free toners, astringents, facial mists, and body bars. "The company still produces witch hazel the old-fashioned way — not distilled," said Reppucci, which means "it contains [about] 195 percent more tannins, which are naturally occurring substances found in the bark and skin of some plants, including witch hazel. Tannins have mild antioxidant properties and help balance the skin's pH levels, reduce irritation, and serve as one of the best natural acne remedies.

"We steep our witch hazel in warm water for hours, keeping all the beneficial tannins in our formula and not losing them during the distillation process," he added.

Similarly, Thayers included slippery elm extracts in many of its early and current products. Slippery elm is approved by the US Food and Drug Administration as a safe and effective over-the-counter drug ingredient for its soothing, protective, moisturizing, and healing properties.[6] A natural demulcent, it is the active ingredient in Thayers lozenges



Historic Thayers product bottles. From left to right: Blackberry Root Cordial, Cholera Mixture, Senna Laxative Syrup, Soothing Syrup, Valerian Pills, and Honey Anise Syrup.
Images courtesy of Thayers.



Historic advertisement for Thayer's Gold Nutritive. Image courtesy of Thayers.

and dry mouth sprays, which are designed to heal sore throats and stimulate saliva production. These products are created by grinding the inner bark into a powder and then combining it with other ingredients like dextrose, magnesium stearate, and sucrose.[7] Slippery elm is also used in Thayers lip balms as well as Thayers Allergy & Sinus Relief Nasal Mist and Spray.

Today, as demand grows for ingredients that are considered clean and familiar, the company is poised to continue to offer products that resonate with consumers. To that end, Thayers has continued to look for ingredients that fit this model. For example, Thayers Natural Remedies now features a line of skin care products that contain apple (*Malus* spp., Rosaceae) cider vinegar, an ingredient first used by the Romans. Apple cider vinegar is a well-known home remedy for relieving itches from rashes and insect bites,[8] and it is a main component of Thayers Dry and Itchy Skin Relief Soothing Lotion and Soothing Spray. The reason it is effective seems to be that the pH of apple cider vinegar is similar to that of the acid mantle of the skin — the layer of oil and perspiration that helps protect and moisturize skin. Because the pH of apple cider vinegar matches the pH of the skin, the company's blog says that it cleanses gently and doesn't strip the skin of natural oils and acidity that protect and balance it. Apple cider vinegar also contains potassium, which helps address conditions such as eczema.[9]

In addition to developing and introducing new products, Thayers continues to update and improve its existing products, including those with witch hazel. In 1989, for example, the company introduced an alcohol-free version of its witch hazel facial toners, because alcohol can be too harsh to be used as a daily facial care regimen for many people, Reppucci noted. In 2012, Thayers began using certified organic witch hazel for its proprietary extract. The witch hazel is grown exclusively on an organic family farm in Easton, a setting that has since become home to Thayers' corporate headquarters. "Certified organic symbolizes the purity of the ingredient and further underscores the importance of creating natural, beneficial products," said Reppucci.

More recently, the company introduced new witch hazel toners with companion ingredients like coconut (*Cocos nucifera*, Arecaceae) water and aloe (*Aloe vera*, Asphodelaceae). Reppucci noted that "the coconut water is a natural anti-inflammatory that works to fight acne while also hydrating the skin." It has a high vitamin C content, which increases collagen production and brightens and protects the skin from sun damage, he added. The new formula claims to help protect and revitalize skin and comes in three scents: cucumber (*Cucumis sativus*, Cucurbitaceae), lavender (*Lavandula angustifolia*, Lamiaceae), and rose (*Rosa* spp., Rosaceae) petal. The additional ingredients do more than just provide scent. For example, rose petals are full of natural oils that restore and smooth skin and serve as a natural astringent to tighten pores. Cucumber contains antioxidants that help clear clogged pores.[10]

Ultimately, a commitment to both evolution and its past may be the secret to Thayers' longevity, and Reppucci doesn't see that changing anytime soon. "The popularity of [witch hazel and slippery elm] have stood the test of time and remain an integral part of our continuing product development," he said. HG

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Goldenseal
Hydrastis canadensis
Photo ©2018 Steven Foster

PROTECTING Goldenseal

How Status Assessments Inform Conservation

By Leah E. Oliver and Danna J. Leaman, PhD

Summary

A recently published global assessment of the conservation status of goldenseal (*Hydrastis canadensis*, Ranunculaceae) has found that the species is Vulnerable to Extinction (i.e., it faces a higher risk of extinction in the wild throughout its distribution in the United States and Canada than many other species). However, the extinction risk is not yet at the level of Endangered (very high risk of extinction) or Critically Endangered (extremely high risk of extinction). This article explains two complementary conservation ranking methods — the International Union for the Conservation of Nature (IUCN) Red List and NatureServe — and the criteria applied to assess the conservation status of goldenseal. These assessments consider all primary threats to goldenseal conservation, including the impact of habitat loss and other factors, such as domestic and international trade, and propose measures to support in situ and ex situ conservation of this species.

Introduction

In 2017, the IUCN published the first comprehensive global Red List assessment of goldenseal, which concluded that the species is globally Vulnerable, a category that indicates a high risk of extinction in the wild.[1,2] To determine risks of extinction, the IUCN Red List of Threatened Species uses a scientifically rigorous approach that is applicable to all species. It has become a world standard, providing information and analyses on the status, trends, and threats to species in order to inform and catalyze action for biodiversity conservation.[3] The assessment was authored by NatureServe, a nonprofit network of scientists that provides access to and analysis of current data on biodiversity. The 2017 IUCN assessment followed and built on NatureServe's 2012 global ranking update, which classified goldenseal as G3G4 — a range rank that spans G3 (Vulnerable; a moderate risk of extinction) and G4 (Apparently Secure; some cause for long-term concern).[4]

Over the last two decades, the North American herb industry has made substantial efforts to recognize threats to goldenseal populations, raise industry and consumer

awareness about the need for goldenseal conservation, and invest in commercial-scale cultivation of the species.[5-7] However, wild-collectors, cultivators, conservationists, and other members of the herbal community have questioned the rationale for the IUCN and NatureServe conservation assessments and the information on which they are based. This article aims to provide transparency about these assessments by explaining the history, rationale, and challenges behind them, and to explore what the conservation status of goldenseal signifies for the current and future sustainability of this important North American herb.

What is Goldenseal?

Goldenseal is a long-lived, perennial plant that is native only to North America, where it grows in densely shaded, deciduous forests. Naturally growing populations are known to occur in 26 states in the eastern United States, ranging from southern Vermont, west to Minnesota, and south to Georgia, Alabama, and Arkansas. In Canada, naturally growing populations are known to occur only in southwestern Ontario.[1,8] The core part of its range includes the Ohio River Valley states of Indiana, Kentucky, Ohio, and West Virginia.[9,10] There are no state-level or range-wide population estimates for goldenseal, which is typical of most wild-harvested plant species.[11]

Goldenseal appeared in early records of medicinal uses of North American plants.[12] Native Americans and Canadian First Nations have used various parts of this plant — especially the rhizomes and roots — in traditional remedies for cancer, eye ailments, inflammation, digestive problems, pneumonia, and heart problems.[13] European colonists adopted and popularized some of these applications. In the 1900s, increased demand for goldenseal was caused in part by its unfounded reputation for masking illicit or performance-enhancing drugs in urine tests.[14-16] This myth apparently grew from a murder mystery published in 1900 in which goldenseal bitters were erroneously identified as strychnine, which inspired an otherwise unfounded association of goldenseal with chemical testing errors in American folklore.[15,17] Demand for goldenseal has increased over time, as applications have expanded beyond traditional and local uses and interest has been renewed in herbal medicines in North America and internationally.[4,17] More recently, the identification of the alkaloids berberine, hydrastine, and canadine in goldenseal provided a scientific basis for its use in certain conditions.[18]

Goldenseal currently is used mainly as a component of traditional herbal medicine formulations marketed as licensed Natural Health Products (NHPs) in Canada[19] and as dietary supplements in the United States. The export market is relatively small and limited primarily to countries with Western herbal medicine traditions, such as Australia and the United Kingdom. Goldenseal also

Goldenseal *Hydrastis canadensis* Photo ©2018 Steven Foster



is exported to Europe in small quantities for use in two traditional German systems of medicine: anthroposophical medicine and homeopathic medicine (J. Brinckmann email to C. Yearsley, March 17, 2018). The World Health Organization includes goldenseal rhizome (Rhizoma Hydrastis) among materials that have global importance in alternative medicine, with its main use described in pharmacopeias and "well established documents" as a treatment for digestive complaints, in addition to a variety of other traditional uses.[20]

Conservation Concerns

Wild goldenseal subpopulations have declined dramatically due to habitat loss and degradation through forest conversion for agricultural use, urban expansion, road intrusion, and recreational use. Population decline also has been caused by commercial collection that began in the mid-1800s.[17,21] Concerns about the conservation of goldenseal have existed since at least 1884, when American pharmacist John Uri Lloyd (author of the aforementioned murder mystery novel) and his brother, mycologist Curtis Gates Lloyd, observed that goldenseal rhizome harvesting and habitat loss were causing significant declines in goldenseal subpopulations.[22] Botanists' observations from this period onward provide anecdotal and observational evidence of the continued decline and loss of goldenseal subpopulations from habitat loss and degradation and increasing demand for wild-collected rhizomes.[23-39] Approximately 80% of the original forests in New England have been lost to land conversion, which reached its peak during the 1800s.[40] In the Canadian portion of goldenseal's range, less than 5% of its forest habitat remains from pre-settlement times.[8]

In the Canadian portion of goldenseal's range, less than 5% of its forest habitat remains from pre-settlement times.

Although goldenseal was cultivated on a small scale for more than a century throughout its native range, most of its domestic and international trade until the early 2000s came from wild-harvested rhizomes and roots.[10] There have been efforts to account for harvest and trade volumes in national and international trade by using records of phytosanitary certificates issued by the US Department of Agriculture (USDA) and by tracking trends in supply and demand (e.g., using wholesale prices published in US herb catalogs).[39] However, in the absence of any official monitoring and reporting requirements, it was not possible to accurately quantify the volumes of roots harvested, traded in domestic markets, or exported from North America.[5,41]

Subpopulations in Canada were first assessed as Threatened in 1991 by the Committee on the Status of Endangered Wildlife in Canada (COSEWIC).[42,43] By the mid-1990s, goldenseal in the United States was considered Critically Imperiled, Imperiled, or Uncommon in 17 of the 26 states in which it occurs.[39,44] According to Bannerman (1997), wild harvest was prohibited in a number of states due to concerns about population decline.[5]

Herbalists also are concerned. United Plant Savers (UpS), a nonprofit organization dedicated to the conservation of native American medicinal plants, included goldenseal in its original list of "Species At-Risk" that identified plants in decline due to expanding popularity and shrinking habitat and range. This list was created in 1997 by "concerned herbalists and conservation-minded plant enthusiasts" to encourage practical and educational programs and to promote organic cultivation of "At-Risk" herbs.[6,45]

CITES Listing

In 1997, the North American office of TRAFFIC: The Wildlife Trade Monitoring Network formally petitioned the US Fish and Wildlife Service (USFWS) to propose goldenseal for inclusion in Appendix II of the Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES).[17] The proposal was adopted at the 10th meeting of the Conference of the Parties to CITES in June 1997.[39] While conservation experts and officials in importing countries were concerned that supplies of goldenseal would fall and prices would rise if goldenseal were included in Appendix II, the conference decided to adopt the proposal.

Goldenseal was listed in Appendix II on September 18, 1997, with an annotation to focus on trade in "whole and sliced roots and parts of roots, excluding manufactured parts or derivatives such as powders, pills, extracts, tonics, teas and confectionary." This listing means that all international exports and re-exports of goldenseal roots and rhizomes, whether wild, forest-grown, or cultivated, require permits issued by the CITES Scientific Authority to enable monitoring and control of materials and volumes in international trade. A CITES export permit signifies that the transaction is legal and does not threaten the species' survival in the wild.[46] Obtaining a permit to export goldenseal also requires proof that the roots, rhizomes, or seeds came from legally acquired parental material and from plants that were at least four years old.[47]

Increased export of powdered goldenseal roots and rhizomes from the US after 1997 made it difficult to monitor international trade[48,49] and led the USFWS to amend the annotation for goldenseal in 2007 to include "underground parts (i.e., roots, rhizomes): whole, parts and *powdered*,"[49] (emphasis added) so that all of the major goldenseal products in international trade could be monitored.

Inclusion of goldenseal in Appendix II stimulated industry investment in research and education campaigns supporting commercial cultivation of the species.[5] For example, propagators and growers worked for more than a decade to improve seed stratification requirements of goldenseal so that the germination rate would support sexual propagation (E. Fletcher email to C. Yearsley, March 21, 2018). The herbal industry also implemented measures to track wild and cultivated production.[6,7] Although nearly all material in trade continued to come



Goldenseal
Hydrastis canadensis
Photo ©2018 Steven Foster

from wild collection until the early 2000s, there has been a shift in the international market to cultivated sources in recent years.[50-52] The CITES Trade Database (2000-2016) indicates that the majority of material in international trade is now from artificially propagated plants. Industry surveys of raw herbal materials producers in the United States undertaken by the American Herbal Products Association (AHPA), a trade association for the US herb industry, documented an increase in cultivated goldenseal roots and rhizomes (compared to wild-collected materials) from a low of 2% cultivated in 1998 to a high of 41% cultivated between 2000 and 2010.[51,52]

Although CITES and industry trade data indicate that cultivated goldenseal makes up an increasing portion of international trade, the most recent publicly available AHPA survey data from 2010 suggest that the majority of goldenseal raw material in US domestic trade was sourced from wild collection. For example, in 2010, 59,197 pounds of goldenseal root and rhizome and 10,791 pounds of leaf were reported from wild sources, while cultivated sources accounted for 17,931 pounds of root and rhizome and 782 pounds of leaf.[51,53]

History, Rationale, and Challenges behind the Recent NatureServe and IUCN Conservation Status Assessments

The transition of international trade of goldenseal from wild-harvested to cultivated sources has had an impact on goldenseal conservation. In 2012, the US CITES Scientific Authority, part of the USFWS, initiated a status review of the species. USFWS engaged NatureServe to carry out the review, with a focus on filling gaps in information about goldenseal's abundance, population trends, life history, core range states, and current threats, particularly the impacts of ongoing wild harvest. This new information was used to update NatureServe's state, national, and global rankings for goldenseal and to complete a global (United States and Canada) IUCN Red List assessment of this species.

The CITES Scientific Authorities in the United States and Canada rely on these and other data sources to determine whether international trade is detrimental to the survival of the listed species. This determination is referred to as a non-detriment finding (NDF). Although CITES permits and monitoring focus on material in international trade, for the purposes of making an NDF, the Scientific Authority "should consider the volume of legal and illegal trade (known, inferred, projected, estimated) relative to the vulnerability of the species (intrinsic and extrinsic factors that increase the risk of extinction of the species)," and, "in considering whether an export may be detrimental, the sustainability of the overall harvest will usually be a necessary consideration."[54]

Methods and Processes of the Conservation Assessments

Information from scientific literature and databases was collated to update the population status and threat information already contained in NatureServe's central databases and in IUCN's Species Information Service (SIS), the database used to compile and manage Red List assessments. NatureServe carried out formal status assessments based on both NatureServe's global ranks[55] and IUCN's Red List categories and criteria.[2] Each assessment entailed compiling

Conservation Status Assessments

Conservation status assessments are key to ensuring the implementation of appropriate conservation measures. These unbiased metrics of conservation condition are used to identify which species are most at risk of extinction, and are separate from governmental regulation and policy. For example, analyses of NatureServe's data have repeatedly shown that the number of species listed under the US Endangered Species Act is an order of magnitude less than the number of at-risk species in the United States — a disparity that stems largely from politics and lack of resources.[57] As a result, federal and subnational (i.e., state or provincial) organizations and government agencies in the United States and Canada rely on NatureServe's status assessments, called "ranks," for conservation prioritization. Internationally, the IUCN Red List assessments are the most widely used methodology for conservation prioritization.

NatureServe Ranks and IUCN Red List Categories

NatureServe is a nonprofit biodiversity conservation organization made up of a network of more than 80 Natural Heritage Programs in the United States and Latin America, and provincial or regional Conservation Data Centers in Canada. The NatureServe Network collects comprehensive information about imperiled species and entire ecosystems, transforms the data into knowledge products and visualizations, and provides meaning through expert analyses to guide decision-making, implement action, and enhance conservation outcomes. NatureServe rankings are undertaken on three geographic scales: Subnational (S ranks), National (N ranks), and Global (G ranks).

The IUCN Red List is organized and published by the IUCN with assessments contributed by a large network of expert specialist groups, Red List authorities, and Red List partners. It is considered to be the global standard for conservation status assessments. Red List assessors assign a category of extinction risk using a rule-based system of criteria and thresholds that accommodate both data-poor and data-rich species. Assessment categories and criteria are applied on a global scale,[1] with adjustments for national- and regional-scale applications.[58]

NatureServe's ranks and Red List assessments consider similar factors related to each species' distribution, threats, and trends, but weigh and evaluate the data differently (Table 1).[59,60] These differences produce complementary interpretations of extinction risk and provide users with nuanced perspectives to make informed conservation decisions. Recent publications have compared the two systems and provide a more detailed overview of the similarities and differences.[59,61] Both systems



Goldenseal
Hydrastis canadensis
Photo ©2018 Steven Foster

enable assessors to objectively apply rules for conservation status assessments. The IUCN Red List assessments require two external reviewers of content, information quality, and consistency with the Red List methodology.

As the North American Red List Authority for plants and a Red List partner institution, NatureServe has years of experience applying Red List criteria to assess species. Similarity between the two systems makes it more cost-efficient to assign Red List categories and global ranks at the same time rather than separately. NatureServe's database is broadly compatible with IUCN's Red List database, the Species Information Service (SIS), so the information can be shared across platforms.

A species assessment is considered a snapshot in time, or a reflection of the knowledge available when the species was assessed. Due to changing threats, conservation actions, and natural events, the conservation status of a species can change over time. Consequently, conservation status must be regularly reviewed. NatureServe and the Red List both recommend that assessments be updated at least once every 10 years.

Data Uncertainty and Risk Tolerance

The incompleteness and imperfect quality of available information that is considered relevant to extinction risk and the potential for assessors to be biased toward more precautionary (i.e., risk-averse) assessments are common concerns about assessing the conservation status of species. These concerns are valid because complete population data are not available for most plant species, and there is evidence suggesting that the tolerance of risk (i.e., a tendency toward lower or higher levels of risk in assessments) is most inconsistent for valuable, exploited species.[62]

Conservation status assessments for valuable, exploited species often require more and higher-quality data, and are more rigorously reviewed, so that the burden of proof is more stringent than assessments for less-valued species. To this end, NatureServe's ranks and Red List assessments have standardized methods and tools to address uncertainty so that the resulting rank or category is comparable to those of other species. Additionally, NatureServe and the IUCN Red List have steps built into their assessment methodologies to reduce the potential for bias. NatureServe assessors, for example, are required to use a rank calculator that weighs factor information and determines a rank. The IUCN Red List requires consistency checks and two reviewers who are knowledgeable about the species and the Red List process. Both NatureServe and Red List assessments can be updated with new information or a new interpretation of existing information.

information relevant to understanding the risk of extinction for a species: geographic distribution; population size; number, size, and distribution of subpopulations; population and habitat trends; type and scale of threats; and existing conservation actions.

Although published literature contains a wealth of useful data about conservation status factors, active field researchers have the most current information about the status of wild populations. In 2012, the NatureServe team contacted botanists at state and federal agencies, natural heritage programs, and universities, among other experts, to gather information on factors contributing to goldenseal's conservation status. NatureServe engaged these botanists by distributing a survey that included questions about goldenseal's distribution on state, federal, and private lands, and protection and regulation on those lands. A section of the survey focused on information about population size, viability, and evidence of wild collection. Additionally, botanists were asked for information about cultivation and wild collection in each state.

The synthesized data from the scientific literature and expert surveys provided higher quality and more current rank factor values, which were entered into NatureServe's global rank calculator and IUCN's Red List assessment. Draft assessments using both the NatureServe rank calculator and IUCN's SIS were completed and peer reviewed.

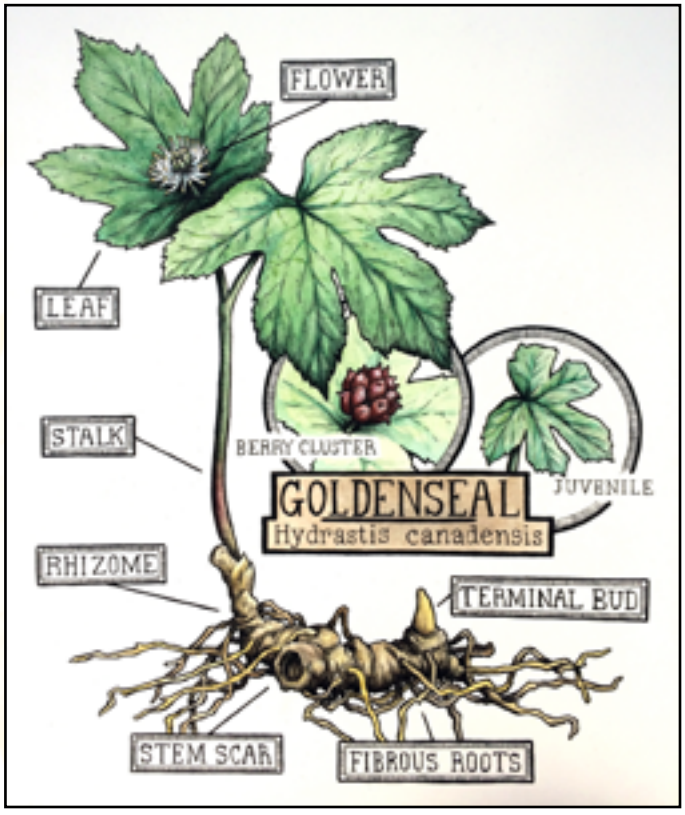
The 2017 IUCN assessment is based on indicators that goldenseal's population has declined by at least 30% over the past three generations of the plant.

Results of the Assessments

NatureServe previously assessed goldenseal's global population as Apparently Secure (G4), indicating that the species is uncommon but not rare, and that there is some cause for concern due to decline over the long term.[1,4] The updated global conservation status of goldenseal using NatureServe's rank calculator and ranking guidance is Vulnerable/Apparently Secure (G3G4), which suggests that there is uncertainty about which of these two ranks (G3 or G4) best reflects the available information about the species.[1,4,55] The G3 rank indicates that the species' status may have declined to Vulnerable (i.e., at moderate risk of extinction due to a restricted range, relatively few subpopulations or occurrences, or recent and widespread declines or other threats).[55,56] Due to uncertainty about ongoing loss of habitat, population estimates across the species' range, and actual levels of wild collection for the domestic market, G3G4 is believed to convey the most accurate extinction risk for goldenseal. Based on the available biological and trade information, including the NatureServe assessment, goldenseal remains in Appendix II of CITES so that international trade does not reduce the wild population to a level that would threaten its survival.

The first IUCN Red List global assessment of goldenseal from 2017 determined that the species is Vulnerable.[1] This category indicates that it faces a higher risk of extinction in the wild throughout its distribution than many other species, but that the extinction risk is not yet at the level of Endangered or Critically Endangered.

The 2017 IUCN assessment is based on indicators that goldenseal's population has declined by at least 30% over the past three generations of the plant and the assumption that this trend will continue in the absence of more effective conservation measures. The indicators of population reduction include: inferred population decline based on firsthand observations in some subpopulations[10,11,63]; suspected population decline based on observed and estimated declines in habitat availability and quality[8,21,23]; and suspected population decline based on observed harvest impacts and suspected levels of exploitation.[23] Suspected levels of exploitation also were based on increasing numbers of requests for wild-harvest permits for goldenseal, as reported by the Indiana Natural Heritage Program. Adequate evidence was available to determine that, in the recent past, the area occupied by all known subpopulations has declined within goldenseal's native range, habitat quality has declined, and exploitation of wild subpopulations has



Goldenseal (*Hydrastis canadensis*) plant structure illustration by Philippe Grenade XIV.
Artwork courtesy of United Plant Savers.

Table 1. Comparison of NatureServe Global Ranks and IUCN Red List Threat Categories[59,60]

	IUCN Red List Category	NatureServe Global (G) Rank	Definitions
EXTINCT	Extinct (EX)[a]	Presumed Extinct (GX)[b]	a No reasonable doubt last individual has died [after] exhaustive surveys. b Not located despite intensive searches; virtually no likelihood of rediscovery.
	Extinct in the Wild (EW)[c]	Presumed Extinct in the Wild (GXC)[d]	c Species known to survive only in cultivation or captivity, or as naturalized population(s) well outside past range. d Presumed extinct in the wild across entire native range, but extant in cultivation, in captivity, as naturalized population(s) outside historical native range, or as a reintroduced population not yet established.
THREATENED	Critically Endangered (CR) (Possibly Extinct)[e]	Possibly Extinct (GH)[f] Possibly Extinct in the Wild (GHC)[g]	e Likely already extinct, but confirmation is required. f Known only from historical occurrences but still some hope of rediscovery. g Possibly extinct in the wild across entire native range, but extant in cultivation, in captivity, as naturalized population(s) outside historical native range, or as a reintroduced population not yet established.
	Critically Endangered (CR)[h] Endangered (EN)[i]	Critically Imperiled (G1)[j]	h Best available evidence indicates that species faces extremely high risk of extinction in the wild. i Best available evidence indicates that species faces very high risk of extinction in the wild. j At very high risk of extinction due to extreme rarity, very steep declines, or other factors.
	Vulnerable (VU)[k]	Imperiled (G2)[l]	k Best available evidence indicates that species faces high risk of extinction in the wild. l At high risk of extinction or elimination due to a very restricted range, very few populations, steep declines, or other factors.
NOT THREATENED	Near Threatened (NT)[m]	Vulnerable (G3)[n]	m Does not meet criteria but is close to qualifying, or likely to qualify, for a threatened category in the near future. n At moderate risk of extinction or elimination due to restricted range, relatively few populations, recent and widespread declines, or other factors.
	Least Concern (LC)[o]	Apparently Secure (G4)[p] Secure (G5)[q]	o Does not meet criteria for threatened (e.g., widespread and abundant taxa). p Uncommon but not rare; some cause for long-term concern due to declines or other factors. q Common: widespread and abundant.
UNKNOWN	Data Deficient (DD)[r]	Unrankable (GU)[s]	r Inadequate information to make direct or indirect assessment of a species' extinction risk based on its distribution and/or population status. s Currently unrankable due to lack of data or substantially conflicting information about status or trends.
	Not Evaluated (NE)[t]	Unranked (GNR)[u]	t Not yet evaluated against the criteria. u Global rank not yet assessed.
	(No IUCN Red List equivalent)	Not Applicable (GNA)[v]	v Conservation status rank not applicable because species is not a suitable target for conservation activities.

reduced the number of individuals. These are continuing threats.

Assessment Challenges Related to Population Size and Trends

Knowledge of population biology and trends for goldenseal is more extensive than for many native species of medicinal herbs, yet estimating the total number of individuals and the rate of population decline for goldenseal is challenging because of its widely scattered distribution, relatively long generation length for an herbaceous plant, clonal habit of reproduction, and the absence of high-quality population monitoring and genetic diversity data.

Scattered Distribution

Anecdotal information from historical documents indicates that goldenseal subpopulations have declined significantly throughout its range since the early 1800s, but little quantitative trend data are available for the last 30 years (approximately three generations).[64] Botanical accounts of goldenseal since the mid-1800s describe dramatic reduction of once-abundant subpopulations to isolated, scattered patches in parts of its range, and attribute these declines to habitat destruction, collection for medicinal uses, and increasing pressure on managed and previously unharvested subpopulations.[21,23,25,65] Declines in goldenseal subpopulations have been qualitatively documented in New York, West Virginia, and Indiana (P. Harmon personal communication to L. Oliver, November 28, 2012; C. Floyd email to L. Oliver, November 30, 2012).[40,63] Fewer subpopulations, patches per subpopulation, and ramets (genetically identical individuals of clonal species) per patch provide additional evidence of subpopulation decline.[63]

Generation Length

The most significant challenge in determining the IUCN Red List assessment ranking of Vulnerable was providing evidence that goldenseal population decline has been and will continue to be at least 30% over three generations. According to the IUCN Red List Guidelines, "generation length should be averaged over asexually and sexually reproducing individuals in the population, weighted according to their relative frequency" in the population.[64] Because these parameters are unknown for goldenseal (as indeed they are unknown for most plant species), it is accepted practice to estimate generation length as the age at first flowering and fruiting, believed to be seven to nine years for goldenseal.[66] (An expert reviewer of this article noted that there are instances of goldenseal's life cycle being three to four years in cultivation settings.) The IUCN assessment, however, eventually settled on an estimated generation length of 10 years.

Clonal Reproduction

Like many plant species, goldenseal reproduces both sexually and clonally, but this mixed-mating system makes it difficult to visually distinguish genetically distinct individuals from clonally identical individuals (ramets) in a population. Sanders (2004) described goldenseal subpopulations as forming "dense patches of a few to greater than 1,000 ramets with patches frequently sparsely distributed across the landscape, such that many patches are isolated from others by great distances."[67]

Plant species that reproduce clonally create a baffling situation for field biologists attempting to count or estimate numbers of reproductive individuals in a subpopulation or the total population. The count of ramets (individual stems in a clone) and estimates of subpopulation sizes overestimate the number of genetically distinct individuals and genetic diversity in the population because the ramets of each clone are genetically identical. Goldenseal ramets have a single stem, so it is not possible to visually differentiate genetically distinct individuals.

The current IUCN Red List guidance recommends that assessors define an individual as the smallest entity capable of independent survival and reproduction (sexual or asexual),[64] but this guidance does not adequately account for concerns about limited genetic diversity within and between such populations that cannot be equated to species that reproduce only sexually (e.g., mammals).

Genetic Diversity

Several recent studies have begun to fill a long-standing gap in information about the genetic diversity of goldenseal. Torgerson (2012) reported low genetic variation across subpopulations examined in North Carolina.[68] In a study that compared the genetic variation between cultivated and natural populations of goldenseal in Ohio, Pennsylvania, West Virginia, and North Carolina, genetic diversity in both settings was found to be low.[69] Six cultivated and 11 wild subpopulations shared a high degree of genetic similarity, which is not surprising, the authors noted, given that the original plants in cultivation were propagated from wild genetic material.

For most crop species, plants in cultivation typically have far less genetic diversity than those in the wild, but this may not be the case for goldenseal. Preliminary evidence, based on small sample sizes, suggests that goldenseal's genetic diversity is low both in the wild and in cultivation.[69,70] Wild subpopulations for most crops are genetic reservoirs that can be accessed to breed disease resistance or environmental tolerance (e.g., drought resistance) into cultivated stock. Overall, low genetic diversity in wild populations means there is less adaptive capacity for environmental stressors, disease, and other pathogens for both wild and cultivated plants.

High genetic diversity that is spread across subpopulations implies frequent gene flow from pollination events among the subpopulations. In contrast, if genetic diversity is higher within a subpopulation than among them, this suggests that the subpopulations are genetically isolated from one another, with little pollination occurring among them. Goldenseal follows the latter scenario. Inoue et al. (2013) found the highest levels of genetic variation within subpopulations, and low genetic similarity across subpopulations.[69] These results support the hypothesis that goldenseal subpopulations are isolated from one another, and that pollen exchange among subpopulations occurs with limited frequency.[67]

Habitat Loss, Population Extirpations, and Decline in Habitat Quality

Recognizing that complete information about population size and trends is lacking for many species, the IUCN Red List criteria are designed to support the use of other types of information, such as inference of long-term and short-term population reductions from observed declines in the area occupied by species subpopulations and in the number of subpopulations or occurrences.[64] Observations of substantial long-term decline of goldenseal's forest habitat since the early 1800s contributed to the conservation concerns that led to the listing of goldenseal in CITES Appendix II. While the pace of land conversion has slowed since then, habitat loss remains a threat to goldenseal throughout its range. These ongoing threats have been corroborated by personal communications with more than a dozen natural heritage botanists from 12 US states with goldenseal populations.[8]

Another source of information used in the conservation status assessments was data on population extirpations (local extinctions) in the heart of goldenseal's range. In Ohio, a state in the core of the species' range, a study by Mulligan and Gorchov (2004) found that nine of 71 historical occurrences were extirpated.[21] Of the 42 goldenseal sites documented in Ohio from 1977-1998, 14 sites were extirpated as of 2002. If the rate of extirpation is assumed to be constant, approximately 1.6% of goldenseal subpopulations are extirpated each year in Ohio, amounting to an approximately 30% decline in the number of subpopulations over a 20-year period (D. Gorchov email to L. Oliver, November 1, 2012).[21] The observed rate of extirpation of goldenseal occurrences in Ohio is likely to be about the same or higher in states on the periphery of goldenseal's distribution, where subpopulations are smaller and more scattered. This rate of decline meets the threshold criterion for the IUCN Red List category Vulnerable, inferring from the estimated rate of subpopulation decline an overall population reduction of at least 30% over the past three generations (21-28 years).[1,2]

Mulligan and Gorchov determined that only 13% of documented extirpations in Ohio were due to deforestation, which suggests that threats other than land conversion caused most of the observed extirpations of goldenseal subpopulations.[21] Decline in the quality of goldenseal habitat also results from ongoing impacts of agricultural expansion, urbanization, recreational use of forests, and road building and maintenance. Other threats leading to habitat degradation include loss or disturbance by flooding and/or fire, invasive species, trampling,[8,71] and browsing by deer.[21]

Population Impacts of Wild Collection

Continuing decline in the global goldenseal population resulting from habitat threats is exacerbated by wild collection. Mulligan and Gorchov attributed 10% of the observed rate of decline in goldenseal subpopulations in Ohio to wild harvesting.[21] They also noted that goldenseal subpopulations in Ohio are smaller, with fewer flowering plants than goldenseal subpopulations in Ontario, and suggested that the difference may be attributed to wild collection being permitted in Ohio and prohibited in Ontario. Christensen and Gorchov (2010) observed that goldenseal harvesters usually collect rhizomes of the largest individuals. They explain that this practice, over time, results in smaller subpopulation sizes and smaller proportions of large, reproductive individuals by adversely affecting population regeneration through both sexual and asexual reproduction.[10]



Goldenseal
Hydrastis canadensis
Photo ©2018 Steven Foster

The volume of wild goldenseal rhizomes and roots exported from the United States and Canada has been monitored and documented based on CITES permit data since the end of 1997 in compliance with these countries' obligations as signatories of CITES.[52] These trade data indicate that wild-harvested goldenseal material has substantially declined relative to the increasing supply of cultivated material in the international market. As mentioned previously, herbal industry surveys of relatively small numbers of primary raw material producers of goldenseal documented an average of 40 tons of goldenseal root (wild and cultivated) in trade per year in the United States between 2004 and 2010.[51] These surveys also indicated that 75% of the tonnage of wild goldenseal in US trade from 1999-2010 was wild harvested. In the absence of more comprehensive and systematic monitoring and documentation of wild goldenseal baseline population data and volumes in domestic trade in the United States, the harvest pressure on the wild population is not quantifiable.

There is a need to more adequately assess whether state regulations are sufficient to protect wild populations of goldenseal.

Some illegal wild harvest of goldenseal subpopulations in Canada occurs.[71,72] Wild harvest in some parts of the species' range in the United States is likely increasing, especially where wild collection remains an important source of income and unemployment is high.[47] In Indiana, for example, collection pressure has increased dramatically over the last decade (C. Floyd email to L. Oliver, November 30, 2012).

Current Outlook and Moving Forward

Conservation concerns that led to goldenseal's inclusion in CITES Appendix II in 1997 stimulated research on what is needed for goldenseal to survive in its remaining natural habitat, much of which informed the updated NatureServe ranking in 2012[4] and the first global IUCN Red List assessment in 2017.[1] Without the inclusion of goldenseal in CITES Appendix II and the subsequent shift in the international commercial goldenseal market from wild-harvested to cultivated supply, it is probable that this species would now be more seriously threatened with extinction than it appears to be at present. CITES permit requirements reduce unsustainable wild harvest and promote protection of goldenseal and its habitat, and removing these requirements could eliminate the most effective mechanism currently available to avoid greater extinction risk. Failure of resource managers and the herbal industry to take stronger actions to reduce the main threats — population decline from habitat loss and unsustainable levels of wild harvest — risks the viability of the species, commerce, and the livelihoods of those that rely on this resource.

In Situ Conservation

Goldenseal is not listed under the US Endangered Species Act and therefore is not protected under US federal law. Protection within states varies considerably, both in terms of how states designate and protect imperiled plants in general, and goldenseal's protection across the states in which it occurs. The USDA PLANTS database tracks state-level legal protection. In 2018, goldenseal was considered Endangered, Threatened, Vulnerable, or of Special Concern in 12 out of the 26 states in which it occurs.[73] Another measure of species imperilment at the state level is NatureServe's state conservation rankings. According to NatureServe's state ranks, goldenseal is Critically Imperiled or Imperiled in 12 states on the periphery of its range; Vulnerable in seven states, some of which are in the core of its range; and Apparently Secure or Secure in the remaining seven core-range states where it is native.[4] There is a need to more adequately assess whether state regulations are sufficient to protect wild populations of goldenseal. Targeted field studies are warranted to ensure that the population integrity (area occupied and conditions) meets the lower threshold of each state's NatureServe ranking. Field inventory is an ideal method to inform these thresholds; however, they are typically reserved for the "rarest of the rare" species due to limitations in resources. Given goldenseal's economic and medicinal value and the ongoing threats that it faces, states should consider prioritizing goldenseal for field inventory to avoid further decline in its habitat and population.

Many subpopulations throughout goldenseal's range occur on land managed by national, state, local, or private organizations, including some subpopulations within Nature Conservancy preserves. Plant collecting on federal land is either forbidden (e.g., on National Park Service land) or requires permits (e.g., on Forest Service land). Harvest regulations differ from state to state. Some states, such as Pennsylvania, require permits for collection on State Forest land or the written permission of landowners for collection on privately owned land.[74] But harvest and interstate commerce of goldenseal root and rhizome as a botanical commodity remain largely unregulated and unmonitored. The Indiana Department of Natural Resources reported an increased demand for this species and concern that the volume of material exported from Indiana will lead to decline of the species in the state. Plants on public and protected lands need protection from illegal collecting[71] and application of good stewardship practices (e.g., late-season harvest to allow seed dispersal) where collecting is permitted.[74] Existing regulations protecting goldenseal and other non-timber forest products on public and protected lands need to be better integrated into forest and other resource management plans and practices.[75]

Goldenseal was assessed as threatened by COSEWIC in 1991[42] and reassessed as threatened in 2000.[43] Goldenseal has federal protection in Canada under the Species at Risk Act and in the province of Ontario under Ontario's Endangered Species Act. Monitoring undertaken in Ontario in 1998 documented the loss of three previously known subpopulations but an overall stable, or possibly increasing, colony size.[76] A recovery strategy for goldenseal in Ontario was published in 2016 in compliance with federal

and provincial requirements for species at risk, and it recommended measures "to maintain existing populations at sustainable levels."[71]

International trade of wild-collected goldenseal from Canada has not been permitted since the species was listed in CITES Appendix II because all wild harvest is considered by the Canadian CITES Scientific Authority (Canadian Wildlife Service, Environment and Climate Change Canada) to be detrimental to the survival of the Canadian subpopulations. All herbal medicinal products containing goldenseal, whatever their origin, must contain only cultivated material to receive marketing authorization and a product license for commercial sale in Canada.[19]

The NatureServe and IUCN conservation status assessments of goldenseal highlight "habitat depletion as one of the biggest negative impacts on goldenseal" and the need for legal protection "that prevents the destruction of habitat where goldenseal grows natively," according to Ed Fletcher, the director of quality and sustainability at Herbal Ingenuity, a raw material supplier based in Wilkesboro, North Carolina (E. Fletcher email to C. Yearsley, March 17, 2018). Josef Brinckmann, the medicinal plants and botanical supply chain research fellow at Traditional Medicinals, a wellness teas company based in Sebastopol, California, explained that habitat loss through deforestation and land use change threatens "all wild forest plants, including goldenseal. Our last remaining biodiverse forests need to be conserved and expanded through reforestation," he wrote (J. Brinckmann email to C. Yearsley, March 21, 2018). One such example of wild forest conservation is the 379-acre UpS Sanctuary in Rutland, Ohio, and other sanctuaries maintained by UpS members.[77]

Potential for Sustainable Wild Collection

In his monograph on goldenseal published in 2011, herbal expert, photographer, and author Steven Foster wrote, "One of the big questions facing the future of goldenseal is whether there is enough supply, especially of wild-harvested root, to meet the demand."[17] Although loss of forest habitat has been the primary cause of decline of goldenseal over time, the sustainability of wild harvest is also a concern. A conservation assessment of goldenseal prepared by the USDA Forest Service in 2003[78] recommended that "to successfully maintain and increase the existing *Hydrastis canadensis* populations [on Forest Service lands], harvesting should not be allowed."[17]

In 1997, ecologist and educator Joy Bannerman, in an *HerbalGram* article from issue 41, wrote:

> There is presently no scientifically valid guideline for "ethical and sustainable harvesting" [of goldenseal] in the wild since significant aspects of population and reproductive biology are unknown. Statements by herbal companies that such material has been "ethically wildcrafted" or the assurance that such is the case by having collectors or sellers sign a document to this effect is scientifically indefensible at this time.[5]

Since then, however, there has been more research on what goldenseal needs to survive and population dynamics of this species (low instances of seed production, high energetic cost of flowering, low genetic diversity, and small, isolated populations), and work on protocols for sustainable wild harvest of medicinal plants in general also has advanced.[79-82] The herbal industry is in a better position now to demonstrate that goldenseal can be wild harvested sustainably.



Goldenseal
Hydrastis canadensis
Photo ©2018 Steven Foster

The USDA requires implementation of a detailed, audited, and monitored sustainable resource management plan for wild-collected herbs in the United States that are certified as organic under the National Organic Program in compliance with the Organic Wild-crop Harvesting Practice Standard.[83] In addition, AHPA has developed voluntary guidelines for Good Agricultural and Collection Practices (GACPs) that focus on desired quality and long-term sustainability for botanicals in general.[81] AHPA's recommendations include:

- Obtain necessary permits, licenses, and permissions for access to public or private property.
- Choose collection sites that contain "healthy stands of plants growing in their normal range and in large enough quantities for collection to be sustainable."
- Use "collection practices that are appropriate to each species and collection area and that minimize damage to the local habitat."
- Avoid harvest of "species listed as endangered or that are not allowed to be harvested under state regulations due to concerns about over-harvest."
- Collect mature plants "only from stands … that are abundant and healthy, with multiple plants of differing ages (seedling, juvenile, and mature)."
- Use collection practices for specific plant parts "that maintain population stability."
- Use "propagation and regeneration techniques during harvest."
- Use "habitat stewardship techniques during harvest."
- Maintain records "that document information and collection practices that ensure the sustainability of the harvest."
- Ensure all harvested plants are identified correctly.
- Develop a "comprehensive written wild collection plan."

While general guidance on good harvesting practices is a step forward, companies are not required to develop standard operating procedures to implement AHPA's GACP guidelines. There is a significant gap in assurance and rigor between recommendations and audited standards. Species that are at high risk of unsustainable harvest require a management system that includes careful evaluation of sustainable yield, monitoring of harvest impacts, verification of good practices, and traceability from the source to the market.

Species that are at high risk of unsustainable harvest require ... careful evaluation of sustainable yield, monitoring of harvest impacts, verification of good practices, and traceability from the source to the market.

Two verification schemes that focus specifically on these aspects include the FairWild Standard and the Pennsylvania Certified Organic (PCO) Forest Grown Verification Program. The FairWild Standard is an independent, third-party-audited certification program.[80] It is, according to Brinckmann, "arguably the most rigorous voluntary international standard designed specifically for sustainable wild collection of medicinal plants" (J. Brinckmann email to C. Yearsley, March 17, 2018). The FairWild Standard has been implemented in Europe, Africa, and Asia, but not yet in North America.

The PCO Forest Grown Verification Program is a voluntary, third-party-audited certification scheme for non-timber forest products.[84] Although it primarily focuses on organic principles, the program may address some of the sustainability concerns about the effects of non-local plants with limited genetic diversity on wild subpopulations of goldenseal. American ginseng (*Panax quinquefolius*, Araliaceae) root, for example, is currently available with this certification,[85] and a USDA Conservation Innovation Grant was awarded to Rural Action, Inc. and UpS to support the development of Forest Grown Verification standards for goldenseal and several other wild-harvested species in the eastern United States.[86]

Conservation of Goldenseal as a Crop Wild Relative

Techniques for cultivated and forest-grown botanical species have become better known and more accessible (e.g., Davis and Persons 2014),[47] and the positive effect of cultivation on product quality has become better understood.[87] However, little information is available about the degree to which cultivation of goldenseal depends on wild sources of propagating stock (i.e., goldenseal roots, rhizomes, and/or seeds).

The continued growth and viability of commercial goldenseal cultivation, including forest-grown, will rely on the availability of germplasm from genetically diverse and ecologically robust wild sources.[88] Availability of locally adapted germplasm is particularly important for the expansion of forest-grown operations.

Conservation of in situ wild populations of crop species and ex situ conservation of genetically diverse and viable seed and other genetic material (e.g., using tissue culture for clonal species or species with recalcitrant seeds) for propagation are essential to maintaining and improving agricultural production. Wild populations of species in cultivation may have "traits that infer protection from environmental stressors and disease."[61] As molecular and genetic techniques become more cost effective, they can be used to identify and select the desired genetically beneficial traits for crop plants.[61]

Ex situ conservation of goldenseal germplasm and other genetic material is also important for restoration in its natural habitat. US government agencies, led by the Bureau of Land Management, have created a National Seed Strategy to provide plant material for cultivation and restoration of native plant species.[89]

If goldenseal has relatively low genetic diversity within and across its wild subpopulations, as indicated by preliminary studies,[69] a major conservation objective for this species should be to maintain genetic diversity in isolated wild subpopulations (both large and small), and to carefully select and store genetically diverse plants ex situ.[63,69] Additionally, safeguarding the genetic variability of goldenseal will require ensuring the persistence of even the smallest patches until the genetic variability on a regional scale has been established.

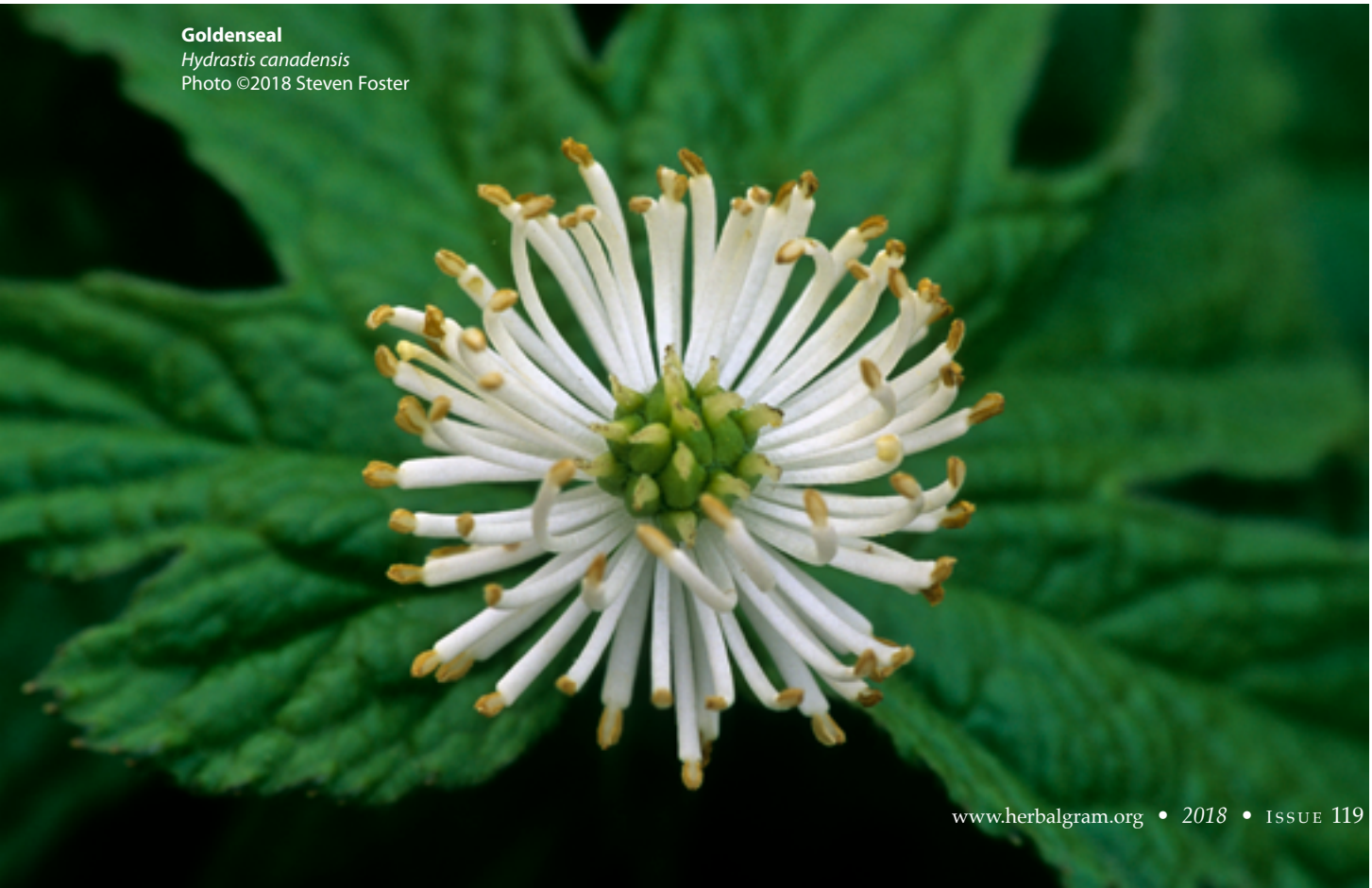
A Path Forward

A successful conservation plan for goldenseal must ensure that the species persists, and it must also satisfy a persistent commercial market. A research, protection, management, and communication plan that focuses on the distribution of goldenseal across the landscape in patches and on the importance of each patch, and that combines the efforts of regulators, resource managers, researchers, industry, and conservationists, offers a way forward. We (the authors) propose an emphasis on:

- Field inventory in key states with the highest reported abundance of goldenseal to verify state conservation status ranks;
- Improved protection of wild goldenseal subpopulations across its remaining distribution;
- Population viability analyses to better understand patch extinction risk, growth, and response to harvest by region;
- Application of a robust monitoring and management system of wild harvest where it can be sustainable, and that builds on traditional, local knowledge and practices of experienced harvesters;
- Adoption of ecologically sound protocols for forest-grown production;
- Use of goldenseal sourced from verifiable and traceable sustainable production systems, whether cultivated, wild-harvested, or forest-grown (and willingness to support related additional costs);
- Genetic studies by region to identify and locate patches with different genotypes;
- Preservation of seed for genotypes identified, and creation of sources of root and rhizome stock for cultivators by region; and
- Use of new kinds of data to track the status of goldenseal, including remote sensing, genetic sampling, citizen science, and social media.

Conclusion

The IUCN Red List and NatureServe criteria and processes are designed to draw upon the best available information about a species to assess the species' risk of extinction. This includes information about a species' population distribution, size, and trends, as well as its ecology, habitat preferences, impacts of threats, and existing conservation actions. Another aim of these complementary assessments is to provide transparency and documentation in the process of assigning a conservation rank. Conservation status assessments of economically important species such as goldenseal can be controversial, given what is at stake: the species' conservation, market demand, and livelihoods of harvesters and others



Goldenseal
Hydrastis canadensis
Photo ©2018 Steven Foster

involved in the industry. However, these risk-ranking protocols have been shown to reliably forecast extinction risk even when there is some degree of data uncertainty.[90]

Neither IUCN Red List assessments nor NatureServe rankings are directly linked to legislative or regulatory responses. Their intended use is to inform the development of policy, legislation, and conservation actions at local, regional, national, and international levels to prevent extinction and improve conservation status.[91] In the case of goldenseal, maintaining monitoring and control of international trade, strengthening monitoring and control of domestic wild-harvest and trade, and improving in situ and ex situ conservation of subpopulations in the United States and Canada will help ensure that this popular medicinal herb continues to be available to the herbal industry and consumers. HG

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Kratom Crackdown: FDA Intensifies Warnings with Limited, Inconclusive Data

To Scientists, Kratom-Linked Salmonella *Outbreak Signals Need for Quality Control, Not a Ban*

By Connor Yearsley

On February 6, 2018, a statement from US Food and Drug Administration (FDA) Commissioner Scott Gottlieb, MD, reiterated the FDA's concerns about the supposed dangers of leaf preparations of the Southeast Asian tree kratom (*Mitragyna speciosa*, Rubiaceae).[1]

"Kratom should not be used to treat medical conditions, nor should it be used as an alternative to prescription opioids," the statement reads. "There is no evidence to indicate that kratom is safe or effective for any medical use."[1]

Kratom is a tropical, evergreen, broad-leafed tree that can grow to 25 meters (82 feet) tall. It is native to peninsular Thailand, southeastern Myanmar, Malaysia, Borneo, Sumatra, the Philippines, and New Guinea. The species belongs to the madder (Rubiaceae) family, a large plant family that also includes coffee (*Coffea arabica*, *C. canephora*). The name "kratom" originates from Thailand and likely derives from the Sanskrit *kadam*, a name that refers to *Neolamarckia cadamba* (Rubiaceae), a widespread tree that is sacred in Hinduism. Similar names are used for various related tree species in the region.[2]

Preparations of kratom leaves have been used for centuries in Southeast Asia for a wide range of purposes, including to treat cough, diarrhea, and diabetes; to manage pain and opioid withdrawal; and to stave off fatigue. Leaf preparations of the plant, including powders and teas, act on the central nervous system. At low doses, they can produce stimulant effects, while higher doses often produce sedative and intoxicating effects.[2]

In a previous FDA statement from November 14, 2017, in which the FDA urged consumers not to use kratom or any compounds from the plant, the FDA claimed it was "aware of reports of 36 deaths associated with the use of kratom-containing products."[3] By the time of the February statement, that number had increased to 44 deaths. Also on February 6, the FDA released reports of the 36 deaths previously noted in November (though only 33 appear to include any data) and stated it would release the remaining reports soon.[1,4-6]

Reports of the 36 deaths "underscore the serious and sometimes deadly risks of using kratom and the potential interactions associated with this drug," according to the FDA.[1] But, in most, if not all, of these cases, kratom's involvement is circumstantial, and it is difficult or impossible to establish a causal relationship between kratom and the deaths. Many of these cases involved other substances and decedents who had a history of misusing substances other than kratom.[4-6] To the FDA, though, this raises concerns that potentially lethal interactions may occur when kratom is used with other substances.[7]

"If you were taking an FDA-approved opioid, you would know exactly what other drugs you're not supposed to be taking with it," an FDA spokesperson was quoted as saying. "We don't have that with kratom — nobody does."[7]

Among the 36 cases was someone who died by suicide after having struggled with bipolar disorder and depression; another who was murdered by a gunshot to the chest; and a third person with nine other substances in his system who fell from a window, suffered a broken arm, and refused medical treatment before dying.[4-6] Also included are nine deaths that occurred in Sweden between 2009 and 2010 that were linked to a product called "Krypton." It has been documented that kratom-containing products sold under the name "Krypton" were also found to contain caffeine and *O*-desmethyltramadol, which is the main active metabolite of the prescription opioid tramadol and is a significantly more potent agonist (activator) of mu-opioid receptors (an opioid receptor subtype that is involved in producing analgesia and euphoria) than tramadol.[2,4-6]

The FDA identified one case that it stated "was of particular concern. This individual had no known historical or toxicologic evidence of opioid use, except for kratom." However, because the February 6, 2018, FDA statement does not include the case ID number, it is unclear to which case report the FDA is referring, or whether the report for this case is even included among those that were released.[1]

It is possible, or perhaps probable, that the FDA was referring to the case of Matthew Dana. In September 2017, Franklin County (New York) Coroner Shawn Stuart ruled that the official cause of death of Dana, a police sergeant from Tupper Lake, New York, who died the previous month, was hemorrhagic pulmonary edema from an accidental overdose of mitragynine, one of the main chemical constituents of kratom. Dana reportedly had an extremely high amount of mitragynine in his blood (3,500 nanograms per milliliter) when he died, but no other foreign substances.[8] "It's possible that we see more people die from drinking too much water every year. Or taking too much Tylenol," Stuart was quoted as saying. "All we're doing is reporting that in this case, kratom was the cause of death."[7] Notably, this case may contradict the frequently mentioned claim that, at high doses, kratom induces vomiting, thus making it difficult to overdose.[2]

Eight of the deaths associated with kratom came from the Center for Food Safety and Applied Nutrition (CFSAN) Adverse Event Reporting System (CAERS), while at least 25 came from the FDA Adverse Event Reporting System (FAERS).[6] Notably, both the CAERS webpage and the FAERS webpage include disclaimers about the limitations of the data.

The CAERS webpage states: "The adverse event reports about a product and the total number of adverse event reports for that product in CAERS only reflect information AS REPORTED and do not represent any conclusion by FDA about whether the product actually caused the adverse events. For any given report, there is no certainty that a suspected product caused a reaction…. The event may have been related to a concurrent underlying condition or activity or to co-consumption of another product, or it may have simply occurred by chance at that time."[9]

Likewise, the FAERS webpage states: "First, there is no certainty that the reported event (adverse event or medication error) was due to the product. FDA does not require that a causal relationship between a product and event be proven, and reports do not always contain enough detail to properly evaluate an event."[10]

The significance of these data perhaps is obscured further because the deaths occurred over at least a nine-year period, and many occurred outside the United States.[4-6] In the United States, kratom started gaining popularity about 15 to 20 years ago.[2] Now, an estimated three million to five million Americans reportedly use kratom regularly. Some kratom proponents contend that, considering this large number of regular kratom consumers in the United States and that people in the plant's native range reportedly have used it safely for centuries,[11] the number of confirmed adverse events is seemingly very low, especially when compared to those caused by other products/substances that are widely available, including some that remain unscheduled under the Controlled Substances Act (CSA) of 1970.[6] Still, kratom is now banned in seven states (Alabama, Arkansas, Indiana, Rhode Island, Tennessee, Vermont, and Wisconsin) and Washington, DC, because of disagreements about its safety and potential for misuse.[2,12]

FDA Calls Kratom 'an Opioid' but Ignores Relevant Scientific Data

The FDA's February 6 statement also describes how a then-unpublished computer model, which the FDA developed, was used to simulate how kratom's constituents "are structured at a molecular level, how they may behave inside the body, and how they can potentially affect the brain." Using this model, FDA scientists evaluated the 25 most prevalent compounds in kratom and concluded: "The model predicted that 22 (including mitragynine) of the 25 compounds in kratom bind to mu-opioid receptors."[1]

Some have questioned the timing of this proclamation and claimed it may be another attempt to stigmatize kratom in light of the current opioid epidemic. After all, the fact that kratom contains opioid-like compounds is not news. This has been known since at least 1996 when an in vivo study on mitragynine was published.[13] The study showed that mitragynine inhibited pain impulses in mice in a dose-dependent manner, and these effects were reversed by naloxone, a semisynthetic opioid receptor antagonist (i.e., an inhibitor of receptor activity) that is used to reverse the effects of opioids in cases of overdose or postoperative sedation.[14] A study published the following year showed that, through the opioid receptor, mitragynine inhibited the movement of isolated guinea pig intestines, and these effects also were reversed by naloxone.[15]

According to Oliver Grundmann, PhD, an associate professor of medicinal chemistry at the University of Florida College of Pharmacy who has co-authored a review of kratom pharmacology, the FDA's computer model considers only whether compounds bind to opioid receptors. "It doesn't take into consideration the data that we have obtained that distinguish the kratom alkaloids mitragynine and 7-hydroxymitragynine from the classical opioids," he said (oral communication, June 4, 2018).

"We know from studies that have been conducted by Christopher McCurdy at the University of Florida and Andrew Kruegel at Columbia University that, after they bind to the opioid receptor, the downstream activation and the downstream signaling are different for the kratom alkaloids," Grundmann continued.[16,17]



Kratom *Mitragyna speciosa*
Photo ©2018 Uomo Vitruviano

That is, the kratom alkaloids do not recruit the beta-arrestin-2 protein that seems, at least partly, to influence respiratory depression and opioid tolerance. Instead, the kratom alkaloids seem "biased" toward the G-protein signaling pathway and therefore do not seem to cause respiratory depression the way that other opioids, like morphine, do.[2,16-18]

David Kroll, PhD, a pharmacologist and medical writer who has written articles about kratom for *Scientific American* and Forbes.com, also noted that "the FDA's computer modeling did not take into account that the 20+ other kratom compounds predicted to have opioid activity are highly unlikely to reach meaningful concentrations in the blood of kratom consumers. The limited published data on kratom in human volunteers suggests that mitragynine may be the only kratom alkaloid that can reach blood levels that would lead to meaningful activity at the mu-opioid receptors" (email, July 24, 2018).

Grundmann added: "I understand that the FDA has safety concerns, but what we have seen so far with kratom is that, for one, the extracts are not being abused in the manner that heroin or morphine or some of the other classical opioids are being abused. They do not seem to be injected. The kratom alkaloids are not being extracted and used as pure substances, like fentanyl or heroin, and then being injected. That is not happening."

In addition, kratom alkaloids are partial agonists of mu-opioid receptors, meaning their maximal effect is lower than that of a full agonist like morphine. The pharmacological actions of the kratom alkaloids more closely resemble those of buprenorphine than those of other, more common opioids. Buprenorphine is a semisynthetic opioid that gradually has been replacing methadone in opioid maintenance therapy for recovering opioid addicts.[2,13,17-18]

"I agree that we need a better system to allow more traditional medicines or supplements, like kratom, to undergo clinical trials," Grundmann added. "There needs to be a pathway for such supplements to be recognized and have a path forward through the regulatory system to be recognized as potential treatment options."

There are countless anecdotal reports of people who claim to have benefitted from kratom. These people have used kratom for a broad variety of purposes, including to cope with post-traumatic stress disorder (PTSD), manage fibromyalgia and other chronic pain conditions, and recover from alcoholism.[2] The FDA, however, is concerned that people are using kratom to self-medicate, without guidance from trained medical professionals.[1,19] Instead, the FDA urges kratom users to seek FDA-approved medications, like methadone, which have undergone extensive review and for which the FDA continuously tracks emerging safety data.[1] Kratom proponents contend that these medications often are inaccessible to the uninsured, don't work for everyone, and can be dangerous.[7] Methadone, for example, causes about 5,000 overdose deaths per year.[2]

While there is hope about the potential for new therapeutics derived from kratom to become safe and effective pain-relievers and opioid recovery aids, there, unfortunately, seems to be little financial incentive to investigate kratom constituents as new drugs. In the United States, the only paths for kratom are as a new dietary ingredient (NDI) or a botanical drug. For NDIs, the FDA requires adequate safety data before the ingredient can be used in supplement products, but the FDA does not believe this requirement has been met for kratom. In addition, no company has submitted the necessary information for a kratom product to become a botanical drug.[2,13]

Herbal products can be sold as long as no disease-treatment claims are made and as long as the FDA does not consider them unsafe. In kratom's case, however, the FDA formally has recommended that the US Drug Enforcement Administration (DEA) place the kratom alkaloids in Schedule I, the most restrictive and punitive schedule, of the CSA.[6,7,19] This, in effect, would mean that possession and distribution of any kratom preparations would be illegal and could result in criminal prosecution. In August 2016, the DEA announced its intention to temporarily place the compounds in Schedule I, but significant backlash from the public and members of Congress convinced the DEA to withdraw that proposal (covered extensively in *HerbalGram* issue 112).[2] Now, the DEA has hinted it could make a decision as early as summer 2018.[19]

"When the FDA comes to us and says a certain substance should be a medicine, we are bound by that," DEA spokesperson Rusty Payne was quoted as saying. "When something is deemed a threat, we act."[7]

On February 8, 2018, two days after the FDA's statement, Grundmann and eight other top kratom researchers submitted a letter to DEA Acting Commissioner Robert W. Patterson and Counselor to the President Kellyanne Conway in which they urged them to consider the effects that banning kratom might have on current kratom users. "We believe strongly that the current body of credible research on the actual effects of kratom demonstrates that it is not dangerously addictive, nor is it similar to 'narcotics like opioids' with respect to 'addiction' and 'death,'" the scientists wrote. "It is our collective judgment that placing kratom into Schedule I will potentially increase the number of deaths of Americans caused by opioids because many people who have found kratom to be their lifeline away from strong opioids will be vulnerable to resumption of that opioid use."[20]

The scientists also claimed that failure to consider possible negative consequences of scheduling would contradict the purpose of the enactment of the CSA (to protect the safety of consumers) and that scheduling would have a "profound and pervasive chilling effect" on additional kratom research.[20]

Salmonella Outbreak

On February 20, 2018, the US Centers for Disease Control and Prevention (CDC) announced it was investigating a *Salmonella* outbreak it claimed was linked to kratom. Twenty-eight people from 20 states were reported to have been infected with a type (or serovar) of *Salmonella* designated I 4,[5],12:b:-. Because whole genome sequencing revealed that *Salmonella* samples from infected individuals were closely related geneti-

cally, the CDC concluded the outbreak likely was caused by a single source. Interviews with some infected people then led the CDC to conclude that kratom was the likely source, even though no kratom products had been shown to be contaminated at the time.[21]

A CDC spokesperson explained: "Health officials use questionnaires to ask sick people in an outbreak what they ate in the week before illness. Eight out of 11 people interviewed reported kratom use, which is a much higher percentage than would be expected for a healthy group of people. That epidemiologic evidence is strong enough to link the outbreak to kratom. There were no other common foods reported at such a higher than expected frequency. In outbreak investigations, it is normal for some people to not report eating the suspected food item, which could be for a variety of reasons. For instance, they might forget what they ate, it isn't specifically asked on the questionnaire, or they got secondary transmission from caring for someone else who was sick."[22]

The *Salmonella* serovar in question reportedly has been found previously in humans, reptiles, and fish, and even in spices and dried mushrooms. Furthermore, a CDC spokesperson confirmed that "*Salmonella* I 4,[5],12:b:- is often seen in countries in Southeast Asia [where kratom is native]. We have seen other outbreaks with this serotype linked to other products, such as frozen shredded coconut and frozen raw tuna."[22]

On March 1, the CDC announced that 12 more people from seven states had been infected with the *Salmonella* serovar in question, bringing the total to 40 people from 27 states. Notably, analyses of leftover and unopened kratom products from ill people in North Dakota and Utah confirmed that both samples were contaminated with the serovar in question.[21]

Two weeks later, the CDC announced that 47 more people from 25 states had been added to the investigation, bringing the total to 87 people from 35 states. Analyses of kratom products from retailers where ill people purchased kratom confirmed that samples were contaminated with additional *Salmonella* serovars. By the end of the investigation on May 24, 199 infected people had been identified from 41 states. Implicated products were recalled, but the investigation was not able to identify a single, common source of contaminated kratom. The CDC warns that contaminated kratom products may still be available for purchase or in people's homes. No deaths were reported.[21]

A group of scientists suggested that, by issuing its kratom import alerts several years ago, the FDA may have inadvertently contributed to the *Salmonella* outbreak, because these alerts significantly reduced the number of available kratom products and thus forced some kratom users to turn to inferior products.[23] In 2012, the FDA issued an import



Kratom
Mitragyna speciosa
Photo ©2018 Uomo Vitruviano

alert notifying field personnel that they could detain kratom-containing products listed in the alert without physical inspection because these products were considered unapproved and/or misbranded drugs. In February 2014, the FDA issued a separate import alert regarding kratom-containing dietary supplements and bulk dietary ingredients.[24]

"This *Salmonella* contamination of kratom products underscores the need for responsible manufacture of products, implementation of current Good Manufacturing Practices (cGMPs) in compliance with the mandatory 2007 rule for dietary supplements, and FDA enforcement, not scheduling [under the CSA]," Paula N. Brown, PhD, director of applied research in biosciences at the British Columbia Institute of Technology, was quoted as saying.[23]

Grundmann also said: "Whenever there is a food contamination, that doesn't mean that all of a sudden we would prohibit lettuce as a food item, for example. That's not happening. If we establish quality control measures for herbal supplements the same way we do for our food chain products, then we can ensure that products consistently meet necessary standards and prevent contamination." HG

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Herbal Supplement Sales in US Increase 8.5% in 2017, Topping $8 Billion

Strongest sales growth in more than 15 years bolstered by continued popularity of Ayurvedic herbs and new formulations of botanicals with general health and nutrition benefits

By Tyler Smith[a], Kimberly Kawa[b], Veronica Eckl[b], Claire Morton[c], and Ryan Stredney[d]

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[b] SPINS; Chicago, Illinois
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[d] IRI; Chicago, Illinois

Introduction

In 2017, retail sales of herbal dietary supplements in the United States surpassed $8 billion for the first time, reaching an estimated total of $8.085 billion. Consumer spending increased by approximately $633 million, or 8.5%, from 2016 — the strongest US sales growth for herbal supplements in more than 15 years. Total US retail sales have increased every year since 2004, and since then, consumer spending on herbal supplements has nearly doubled.

The information presented in this report is based on retail sales data provided by the market research firms SPINS and IRI, both based in Chicago, Illinois, and the *Nutrition Business Journal* (NBJ), part of the New Hope Network, a Boulder, Colorado-based natural products industry-focused media company owned by Informa. SPINS collaborated with IRI to determine total retail sales of herbal dietary supplements in the mainstream multi-outlet retail channel. NBJ calculated total overall sales of herbal supplements as well as breakdowns by market channel and product type (single-herb vs. combination-herb supplements).

In addition to the overall sales growth for herbal dietary supplements, total retail sales increased in all market channels in 2017, according to NBJ estimates. The strongest growth was seen in direct sales of herbal supplements, which totaled $4.012 billion in 2017, an 11.2% increase from the previous year. Mass-market retail sales grew by 8.4% to reach an estimated total of $1.449 billion in 2017, and herbal supplement sales in natural and health food stores, which totaled $2.624 billion in 2017, increased by 4.7% from the previous year.

The SPINS/IRI sales data for individual herbs discussed in this report, and those listed in Tables 4 and 5, reflect sales of dietary supplements in which that herb is the primary ingredient. This includes only products that meet the legal definition of a dietary supplement per the US Food and Drug Administration.[1] The figures in this report reflect the most current estimates (as of July 2018) for herbal dietary supplement sales during the 52-week period that ended January 1, 2018.

Mainstream Channel

According to SPINS/IRI data, mainstream multi-outlet retail sales of herbal dietary supplements totaled $925,935,334 in 2017, a marginal increase of 0.698% from the previous year. The substantial differences between the mainstream sales totals from SPINS/IRI and NBJ can be explained in part by the organizations' differing channel definitions. SPINS, for example, does not include convenience store sales in its mainstream channel data.

For the fifth consecutive year, horehound (*Marrubium vulgare*, Lamiaceae) was reported as the top-selling herbal dietary supplement ingredient in mainstream US retail outlets. In this channel, horehound supplement sales totaled $140,832,190 in 2017, a 12.3% increase from 2016. Records of the medicinal use of horehound for respiratory conditions date back to the first century,[2,3] and the herb is still commonly used for its expectorant and cough-suppressant properties, typically in the form of cough drops and lozenges. (However, according to SPINS, one of the top-selling horehound products in 2017 was in the form of a single-herb extract marketed for respiratory health.)

With a 46.7% increase in sales from 2016, turmeric (*Curcuma longa*, Zingiberaceae) experienced the strongest sales growth in the 2017 mainstream retail channel. Consumers spent a total of $32,456,933 on turmeric supplements in mainstream retail stores in 2017, an increase of roughly $10.3 million from the previous year. This increase in sales earned turmeric a spot as the fifth top-selling mainstream herbal supplement ingredient, up from its 10th-place rank in 2016.

Consumer interest in turmeric has increased substantially in recent years. In its 2016 Food Trends report, Google classified turmeric as the "breakout star" of the functional food movement from 2011 to 2016, with Google searches for the ingredient increasing by 300% during that time.[4,5]

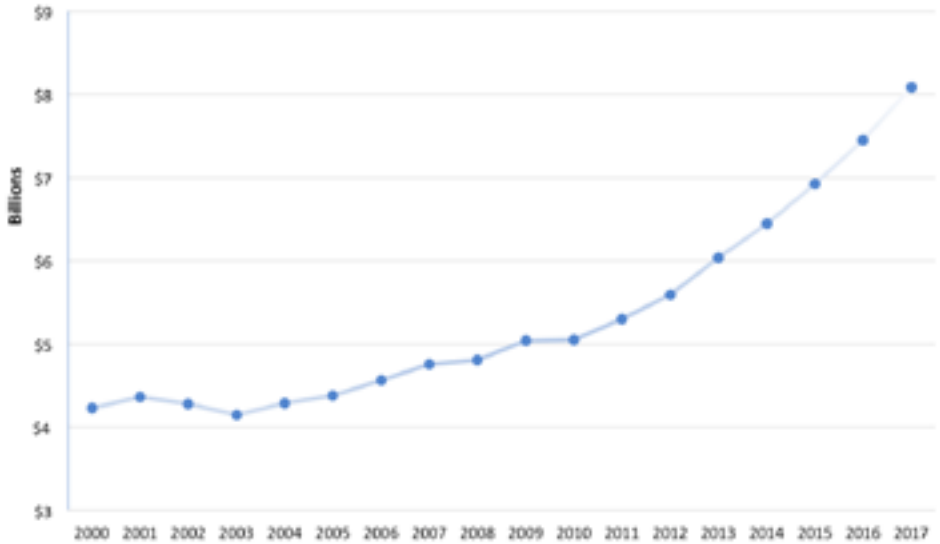
The rise of this golden spice has coincided with increased consumer familiarity with and interest in Ayurveda, a traditional medicine system of India. In addition to being a widely used food ingredient (e.g., in curries), turmeric has

Table 1. Total US Retail Sales of Herbal Supplements*	
2000	$4.225 billion
2001	$4.361 billion
2002	$4.275 billion
2003	$4.146 billion
2004	$4.288 billion
2005	$4.378 billion
2006	$4.558 billion
2007	$4.756 billion
2008	$4.800 billion
2009	$5.037 billion
2010	$5.049 billion
2011	$5.302 billion
2012	$5.593 billion
2013	$6.033 billion
2014	$6.441 billion
2015	$6.922 billion
2016	$7.452 billion
2017	$8.085 billion

Source: *Nutrition Business Journal*

* Includes sales in all channels. NBJ primary research includes NBJ surveys of supplement manufacturers, distributors, MLM firms, mail order, internet, and raw material and ingredient supply companies, as well as numerous interviews with major retailers (Walmart, Costco, etc.), manufacturers, suppliers, and industry experts. Secondary sources include IRI, SPINSScan Natural, Nielsen, *Natural Foods Merchandiser*, Insight, The Hartman Group, company data, and other published material.

Figure 1. Total US Retail Sales of Herbal Supplements



Source: *Nutrition Business Journal* (consumer sales)

been used medicinally in Ayurveda to address a diverse range of health issues, including ulcers, joint pain, skin conditions, inflammation, respiratory conditions, and kidney and liver disorders, among others.[6]

Turmeric sales may have also benefited from the viral popularity of "wellness tonics," which Whole Foods named as one of the top 10 food trends of 2017.[7] Golden milk and turmeric lattes, which typically contain turmeric and other spices added to warmed milk or espresso, were among the year's trending tonics, with major coffee chains such as Starbucks and Peet's adding various turmeric-containing options to their menus in 2017.[8]

According to SPINS, the top-selling mainstream turmeric products in 2017 were marketed for non-specific health conditions. However, mainstream consumers increasingly are seeking condition-specific turmeric supplements, particularly those for joint health, immune health, and pain and inflammation. Modern research on turmeric has largely focused on curcuminoids, a group of biologically active compounds that includes curcumin. Evidence from human clinical trials supports some of turmeric's traditional Ayurvedic uses, including for pain management, gastrointestinal disorders, and skin conditions.[9]

In addition to turmeric, four other botanical ingredients saw sales increases of more than 30% in the 2017 mainstream channel: wheatgrass/barley grass, elderberry, fenugreek, and ivy leaf.

Sales of wheatgrass (*Triticum aestivum*, Poaceae) and barley grass (*Hordeum vulgare*, Poaceae) supplements, which experienced the greatest mainstream sales growth in 2016, grew by 44.2% in 2017. These ingredients likely have continued to benefit from the consumer desire for ingredients with general health and wellness benefits, as discussed later in this report.

Sales of elderberry (*Sambucus nigra*, Adoxaceae) and ivy leaf (*Hedera helix*, Araliaceae), which are typically used to support immune and respiratory health,[10] increased by 34.7% and 30.2%, respectively. Increased sales of these supplements may have been related to the higher-than-average number of flu-like illnesses in the United States from mid-December 2016 to mid-March 2017, as reported by the US Centers for Disease Control and Prevention.[11]

Fenugreek (*Trigonella foenum-graecum*, Fabaceae), an herb traditionally used to stimulate breast milk production, saw an increase in sales of 33.5% from 2016. Multiple human clinical trials published in 2016 and 2017 investigated a range of other

Table 2. US Retail Channel Definitions*

	SPINS/IRI	*Nutrition Business Journal*
Mainstream Channels	**Mainstream Multi-Outlet Channel** In collaboration with IRI. This channel coverage includes the food, drug, and mass-market sector (or "FDM"; supermarkets, drugstores, and mass market retailers), military commissaries, and select buyer's clubs and so-called dollar stores. SPINS/IRI data do not include convenience store sales.	**Mass Market Channel** Mass market includes food/grocery, drug, mass merchandise, and club and convenience stores, including Walmart, Costco, etc.
Natural Channels	**Natural Channel** Includes co-ops, associations, independent retailers, and large regional chains. These data do *not* include sales from natural foods retail giant Whole Foods Market, which does not report its dietary supplement sales to SPINS or other market tracking firms. Only full-format stores with at least $2 million in annual sales (with at least 50% of sales from natural/organic products) are included.	**Natural & Health Food Channel** Natural and health food include supplement and specialty retail outlets, including Whole Foods Market (estimates), GNC, sports nutrition stores, etc.
Direct Sales		Direct sales include internet, mail order (including catalogs), direct mail, and direct response TV and radio; practitioners representing conventional and alternative products selling to their patients, including ethnic and herbal shops; and multilevel marketing (MLM) and network marketing firms.

* The sales discussed in this article pertain only to those involving herbal and other plant-based dietary supplements, and generally do not include herbs sold as teas and beverages or as ingredients in natural personal care and cosmetic products, including so-called "cosmeceutical" products.

potential uses for fenugreek, including for age-related symptoms of androgen decline,[12] menopausal symptoms,[13] and low sperm counts.[14] Sales of fenugreek supplements may have also benefited from the increased familiarity with Ayurveda, in which it has been used traditionally for millennia.[15]

Only three herbal supplement ingredients in the 2017 mainstream channel experienced sales decreases of more than 30%: green coffee (–38.2%), coconut oil (–34.9%), and green tea (–30.4%). Once touted for their weight-loss benefits by the popular daytime television host Mehmet Oz, MD, green tea (*Camellia sinensis*, Theaceae) and green coffee (*Coffea arabica*, Rubiaceae) extracts peaked in popularity in 2014, and their sales have declined steadily since then. This is likely due in part to increased consumer skepticism of weight-loss products, whose marketing claims have been questioned publicly in Senate hearings[16] and consumer education campaigns[17] in recent years. Instead of turning to single-ingredient "miracle" weight-loss supplements, consumers' attitudes toward weight management products appear to have shifted. "Consumers … are taking a more balanced, holistic approach to managing weight as an attempt to improve health," noted Informa Managing Editor Rachel Adams in a recent publication from *Natural Products INSIDER*.[18]

Coconut oil (*Cocos nucifera*, Arecaceae) exploded in popularity in 2013 with a roughly 4,000% increase in sales from 2012, but mainstream sales of this ingredient started to decline in 2016. The continued decline in 2017 may be due in part to a highly publicized Presidential Advisory released in June 2017 from the American Heart Association. The advisory, which suggested that coconut oil was no healthier than beef fat in terms of potential cardiovascular effects, noted: "Because coconut oil increases LDL cholesterol, a cause of [cardiovascular disease], and has no known offsetting favorable effects, we advise against the use of coconut oil."[19]

Table 3. Total Herbal Supplement Sales in US by Channel

	2014	2015	2016	2017	% Change from 2016
Mass Market	$1.116 billion	$1.204 billion	$1.336 billion	$1.449 billion	8.4%
Natural & Health Food	$2.186 billion	$2.356 billion	$2.506 billion	$2.624 billion	4.7%
Direct Sales	$3.139 billion	$3.363 billion	$3.609 billion	$4.012 billion	11.2%

Source: *Nutrition Business Journal*



Horehound
Marrubium vulgare
Photo ©2018 Steven Foster



Black cohosh
Actaea racemosa
Photo ©2018 Steven Foster

Echinacea
Echinacea purpurea
Photo ©2018 James Sullivan

Table 4. Top-Selling Herbal Supplements in 2017 — US Mainstream Multi-Outlet Channel

Rank	Primary Ingredient	Latin Binomial	Total Sales	% Change from 2016
1	Horehound	*Marrubium vulgare*	$140,832,190	12.3%
2	Echinacea[a]	*Echinacea* spp.	$84,700,409	22.9%
3	Cranberry	*Vaccinium macrocarpon*	$68,121,373	–7.9%
4	Ivy Leaf	*Hedera helix*	$32,988,778	30.2%
5	Turmeric[b]	*Curcuma longa*	$32,456,933	46.7%
6	Black Cohosh	*Actaea racemosa*	$32,373,787	–11.3%
7	Garcinia	*Garcinia gummi-gutta* (syn. *G. cambogia*)	$32,298,038	–17.2%
8	Green Tea	*Camellia sinensis*	$30,151,628	–30.4%
9	Ginger	*Zingiber officinale*	$29,532,707	5.2%
10	Fenugreek	*Trigonella foenum-graecum*	$28,823,510	33.5%
11	Flax Seed / Flax Oil	*Linum usitatissimum*	$28,361,026	–11.1%
12	Aloe	*Aloe vera*	$21,139,780	6.3%
13	Yohimbe	*Pausinystalia johimbe*	$19,912,911	–5.0%
14	Saw Palmetto	*Serenoa repens*	$19,294,711	10.8%
15	Elderberry	*Sambucus nigra*	$19,156,461	34.7%
16	Valerian	*Valeriana officinalis*	$17,708,369	–18.2%
17	Milk Thistle	*Silybum marianum*	$16,799,553	-0.6%
18	Garlic	*Allium sativum*	$15,918,006	–1.0%
19	Boswellia	*Boswellia serrata*	$14,638,170	9.7%
20	Senna[c]	*Senna alexandrina*	$13,550,590	17.9%
21	Ginkgo	*Ginkgo biloba*	$13,150,432	1.7%
22	Cinnamon	*Cinnamomum* spp.	$12,140,102	–12.9%
23	Rhodiola	*Rhodiola* spp.	$10,912,343	8.1%
24	Coconut Oil	*Cocos nucifera*	$9,609,631	–34.9%
25	Ginseng[d]	*Panax* spp.	$9,450,098	–2.9%
26	Horny Goat Weed	*Epimedium* spp.	$9,440,726	–1.9%
27	Red Yeast Rice[e]	*Oryza sativa*	$9,419,567	–4.7%
28	Fennel	*Foeniculum vulgare*	$9,374,734	7.3%
29	Guarana	*Paullinia cupana*	$9,099,900	–13.8%
30	Plant Sterols[f]	—	$8,890,234	–27.8%
31	Açaí	*Euterpe oleracea*	$8,523,191	–19.6%
32	Green Coffee	*Coffea arabica*	$8,358,636	–38.2%
33	Wheatgrass / Barley Grass	*Triticum aestivum* / *Hordeum vulgare*	$8,337,413	44.2%
34	Bioflavonoid Complex[g]	—	$8,264,590	–17.9%
35	Yerba Maté	*Ilex paraguariensis*	$6,630,471	–25.8%
36	Maca	*Lepidium meyenii*	$6,250,846	0.0%
37	St. John's Wort	*Hypericum perforatum*	$5,805,384	–3.6%
38	Horsetail	*Equisetum* spp.	$4,028,325	–2.8%
39	Chia	*Salvia hispanica*	$3,857,463	–26.6%
40	Evening Primrose Oil	*Oenothera biennis*	$3,587,133	–4.2%

Source: SPINS/IRI (52 weeks ending January 1, 2018)

[a] Includes three *Echinacea* species: *E. angustifolia*, *E. pallida*, and *E. purpurea*.
[b] Includes standardized turmeric extracts with high levels of curcumin.
[c] Excludes over-the-counter laxative drugs containing senna or sennosides.
[d] Excludes eleuthero (*Eleutherococcus senticosus*), formerly referred to as "Siberian ginseng."
[e] Red yeast rice is fermented with the yeast *Monascus purpureus*.
[f] This category does not include β-sitosterol.
[g] Bioflavonoids are phytochemicals that often are extracted from citrus fruits (e.g., *Citrus reticulata*).

Table 5. Top-Selling Herbal Supplements in 2017 — US Natural Channel

Rank	Primary Ingredient	Latin Binomial	Total Sales	% Change from 2016
1	Turmeric[a]	*Curcuma longa*	$50,346,121	12.2%
2	Wheatgrass / Barley Grass	*Triticum aestivum* / *Hordeum vulgare*	$19,706,608	–6.7%
3	Flax Seed / Flax Oil	*Linum usitatissimum*	$15,320,102	–5.5%
4	Aloe	*Aloe vera*	$14,474,683	2.6%
5	Elderberry	*Sambucus nigra*	$12,452,723	20.6%
6	Ashwagandha	*Withania somnifera*	$10,625,382	25.6%
7	Milk Thistle	*Silybum marianum*	$9,960,892	3.8%
8	Maca	*Lepidium meyenii*	$9,114,769	0.3%
9	Echinacea[b]	*Echinacea* spp.	$9,035,520	11.5%
10	Oregano[c]	*Origanum vulgare*	$8,693,675	19.7%
11	Saw Palmetto	*Serenoa repens*	$7,875,432	11.0%
12	Cannabidiol (CBD)	*Cannabis* spp.	$7,583,438	303.0%
13	Cranberry	*Vaccinium macrocarpon*	$7,155,636	–1.9%
14	Garlic	*Allium sativum*	$6,841,521	16.0%
15	Valerian	*Valeriana officinalis*	$5,891,259	3.5%
16	Echinacea-Goldenseal Combo	*Echinacea* spp. / *Hydrastis canadensis*	$5,866,571	15.7%
17	Mushrooms	—	$5,611,642	29.0%
18	Chlorophyll / Chlorella	— / *Chlorella vulgaris*	$5,444,533	–0.2%
19	Coconut Oil	*Cocos nucifera*	$5,397,873	–23.5%
20	Garcinia	*Garcinia gummi-gutta* (syn. *G. cambogia*)	$5,371,762	18.3%
21	Horsetail	*Equisetum* spp.	$5,370,166	8.1%
22	Ginkgo	*Ginkgo biloba*	$4,731,669	6.2%
23	Nigella	*Nigella sativa*	$4,675,514	202.5%
24	Fenugreek	*Trigonella foenum-graecum*	$3,874,247	2.7%
25	Red Yeast Rice[d]	*Oryza sativa*	$3,864,135	2.4%
26	Quercetin[e]	—	$3,674,159	6.1%
27	Holy Basil	*Ocimum tenuiflorum*	$3,633,776	1.4%
28	Cherry Fruit	*Prunus* spp.	$3,626,819	8.4%
29	Stevia	*Stevia rebaudiana*	$3,470,576	–0.3%
30	Kava	*Piper methysticum*	$3,437,360	10.6%
31	Olive Leaf	*Olea europaea*	$3,294,700	0.6%
32	Ginseng[f]	*Panax* spp.	$3,236,230	5.8%
33	Black Cohosh	*Actaea racemosa*	$3,088,416	–8.5%
34	Evening Primrose Oil	*Oenothera biennis*	$2,871,622	6.6%
35	Ginger	*Zingiber officinale*	$2,823,923	19.8%
36	Kelp	*Laminaria digitata*	$2,772,633	1.4%
37	Moringa	*Moringa oleifera*	$2,738,118	32.9%
38	Rhodiola	*Rhodiola* spp.	$2,686,686	8.7%
39	Hawthorn	*Crataegus* spp.	$2,685,685	9.8%
40	Nettle	*Urtica dioica*	$2,560,574	12.8%

Source: SPINS (52 weeks ending January 1, 2018)

[a] Includes standardized turmeric extracts with high levels of curcumin.
[b] This includes three *Echinacea* species: *E. angustifolia*, *E. pallida*, and *E. purpurea*.
[c] Includes products labeled as containing oregano oil and oregano leaf tinctures.
[d] Red yeast rice is fermented with the yeast *Monascus purpureus*.
[e] Quercetin is a common plant flavonol.
[f] Excludes eleuthero (*Eleutherococcus senticosus*), formerly referred to as "Siberian ginseng."

Table 6. Total US Retail Sales of Herbal Supplements by Product Type			
2014	**Total Sales**	**% of Total Sales**	**% Growth**
Single Herbs	$4.024 billion	62.5%	6.2%
Combination Herbs	$2.418 billion	37.5%	7.7%
2015			
Single Herbs	$4.245 billion	61.3%	5.5%
Combination Herbs	$2.677 billion	38.7%	10.7%
2016			
Single Herbs	$4.505 billion	60.5%	6.1%
Combination Herbs	$2.947 billion	39.5%	10.1%
2017			
Single Herbs	$4.759 billion	58.9%	5.6%
Combination Herbs	$3.326 billion	41.1%	12.9%
Source: *Nutrition Business Journal*			



Ivy
Hedera helix
Photo ©2018 Steven Foster

As in previous years, *HerbalGram* chose to exclude certain ingredients from SPINS and IRI's tally of the 40 top-selling herbal supplements in the US mainstream retail channel. As the only branded supplement on the list, Relora (InterHealth Nutraceuticals Inc.; Benicia, California), a proprietary blend of magnolia (*Magnolia officinalis*, Magnoliaceae) and phellodendron (*Phellodendron amurense*, Rutaceae) bark extracts, was not included in this year's report. Had it been included, Relora would have been the 38th top-selling supplement in 2017, despite a 25.6% decline in sales from 2016.

Natural Channel

According to SPINS, sales of herbal dietary supplements in the US natural channel totaled an estimated $405,153,959 in 2017, an increase of 8.9% from 2016. NBJ, which, unlike SPINS, includes sales from Whole Foods Market in its natural and health food retail channel, determined significantly higher sales of $2.624 billion in this channel. In general, natural channel sales come from so-called "core shoppers," who tend to be committed to a natural lifestyle. "Peripheral shoppers," who typically are less committed to natural products and wellness trends, are more likely to purchase dietary supplements in the mainstream channel.

For the fifth consecutive year, turmeric was the top-selling herbal supplement ingredient in natural retail outlets with sales totaling $50,346,121 in 2017, an increase of 12.2% from 2016. While mainstream consumers primarily purchased turmeric supplements for non-specific health conditions, the greatest sales of turmeric supplements sold in the natural channel were marketed for pain and inflammation. Non-specific health conditions, however, still represented the second largest market share of turmeric supplements sold in this channel, followed by those for joint health and cardiovascular health.

For the first time, cannabidiol (CBD), a naturally occurring, non-intoxicating compound in *Cannabis* species (Cannabaceae), ranked among the 40 top-selling herbal supplement ingredients in the US natural channel. CBD

was the 12th top-selling ingredient in this channel with total sales of $7,583,438 in 2017, an increase of 303% from the previous year.

SPINS has been tracking sales of CBD in both mainstream and natural retail channels since 2016, but the legality of this ingredient remains murky. The US Drug Enforcement Administration considers "marihuana" and "marihuana extracts" illegal under Schedule I of the Controlled Substances Act,[20] but certain allowances were made for the research and limited production of industrial hemp when the Farm Bill of 2013 became law in early 2014.[21] In an effort to avoid potential legal issues, many manufacturers have chosen to produce and market products with only "hemp-derived" CBD.

CBD preparations are perhaps best known for their documented benefits for treatment-resistant epilepsy,* but CBD is "attracting increasing interest as 'a pharmacological agent of wondrous diversity,' with analgesic, anti-inflammatory, antioxidant, antiemetic, anxiolytic," and numerous other documented properties, according to a recent review of CBD claims.[23] The majority of CBD sales in 2017 were attached to products with non-specific health focuses, according to SPINS, but sales of condition-specific CBD formulations, such as those for mood support and pain and inflammation, are beginning to emerge.



Turmeric
Curcuma longa
Photo ©2018 Steven Foster

Nigella (*Nigella sativa*, Ranunculaceae), also known as black cumin or black seed, also experienced significant sales growth in 2017. Retail sales of nigella rose by 202.5% from 2016, making it the 23rd top-selling herb in this channel. According to SPINS, liquid seed oil preparations with non-specific health focuses made up the majority of nigella supplement sales in both natural and mainstream retail stores in 2017.

Archeological evidence suggests that nigella has been used as a food and medicine since the third millennium BCE, and the herb is still commonly used in traditional medicine systems in Asia. In Ayurveda, dried nigella seeds are used to treat various digestive issues (e.g., gas and diarrhea), and in the Unani system of medicine, nigella is used to treat a range of conditions, including asthma, migraine, joint and back pain, and skin diseases. Evidence from human clinical trials suggests that nigella preparations may have some benefits for respiratory conditions, rheumatoid arthritis, and functional dyspepsia.[24]

Moringa (*Moringa oleifera*, Moringaceae), which also made its debut among the 40 top-selling herbs in the natural channel in 2017, was the only other ingredient with an increase in sales of more than 30% from 2016. Moringa, like nigella, is a botanical commonly used in Ayurvedic medicine that has general health and nutrition benefits.

* In June 2018, the US Food and Drug Administration approved a CBD oral solution (Epidiolex; GW Pharmaceuticals; Cambridge, United Kingdom) for two forms of rare, treatment-resistant epilepsy that mostly affect children.[22] This is the first time the FDA has approved a drug containing a substance derived from cannabis.

Also known as horseradish tree (not related to the spice horseradish [*Armoracia rusticana*, Brassicaceae]), moringa is cultivated and consumed widely in South Asian countries. The leaves are rich in protein, beta-carotene, vitamin C, calcium, and potassium, and various plant parts have been used traditionally in India to treat inflammation and infection, as well as gastrointestinal, cardiovascular, and liver conditions.[25] According to SPINS, powders made up the majority of moringa supplement sales in the 2017 natural channel.

Consumers suffering from "pill fatigue," who increasingly are looking for ingredients with general wellness and nutrition benefits in alternative delivery forms (e.g., powders and liquids), likely contributed to the sales growth of nigella and moringa in 2017.[26] In addition, the herbs' long history of use in Ayurveda may have added to their appeal, particularly for core consumers in this channel who tend to be more familiar with natural product trends. Several other botanicals with traditional Ayurvedic uses experienced sales growth in the natural channel, including ashwagandha (*Withania somnifera*, Solanaceae; 25.6%), ginger (*Zingiber officinale*, Zingiberaceae; 19.8%), and garlic (*Allium sativum*, Amaryllidaceae; 16%).[27]

Coconut oil was the only ingredient in the 2017 natural channel with a significant decline in sales (–23.5%).

Direct Sales

Direct sales of herbal supplements increased by 11.2% from 2016, reaching an estimated $4.012 billion in 2017, according to NBJ. This is the strongest percentage sales growth in this channel in more than a decade, and the first time since 2012 that growth in the direct sales channel outpaced that of the mainstream and natural/health food channels. Direct channel sales of herbal dietary supplements include multilevel marketing companies (also known as network marketing companies). This channel also encompasses mail- and internet-order sales companies, direct-response TV and radio sales, and sales by health practitioners.

Single-Herb vs. Combination-Herb Supplements

For the seventh consecutive year, sales growth of combination-herb supplements was stronger than that of single-herb supplements. Across all channels, sales of combination-herb supplements increased by 12.9% from 2016, and sales of single-herb supplements increased by 5.6%. Combination-herb formulas generally are intended for more specific uses than single-herb supplements. Despite the continued growth for combination-herb products, single-herb supplements have composed the majority of overall sales for more than a decade.

Conclusion

After the highly publicized and controversial campaign against certain herbal supplements led by the New York attorney general in 2015, the natural products industry entered a period of self-reflection. Since then, many responsible members of the dietary supplements industry have taken significant steps to regain consumer trust by improving transparency along the supply chain, enhancing traceability of raw botanical materials, and bringing attention to ingredients with potential adulteration concerns, among other efforts. The record 8.5% growth in herbal supplement sales in 2017 suggests that these efforts may be paying off. Sales in both natural retail outlets and mainstream stores reflect heightened consumer interest in once-obscure botanicals and medical traditions. Increased familiarity with Ayurvedic herbs, new formulation options, and consumer demand for culinary botanicals with general health and nutrition benefits continued to drive sales of these products in 2017. HG

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Cranberry
Vaccinium macrocarpon
Photo ©2018 Steven Foster

The Wildcrafting Brewer: Creating Unique Drinks and Boozy Concoctions from Nature's Ingredients by Pascal Baudar. White River Junction, VT: Chelsea Green Publishing; 2018. Softcover, 304 pages. ISBN: 9781603587181. $29.95.



The Wildcrafting Brewer, the gorgeous new book by Pascal Baudar, can be described with three simple words: herbs, fermentation, and terroir. In this book, Baudar has brought together the knowledge of a wildcrafter with the intuition of a shaman and the inspiration of a madman. *The Wildcrafting Brewer* stands out because of its amazing pictures and clear information about creating unique beers, meads, and wines at home.

Pascal Baudar is a culinary alchemist, food lover, wildcrafter, experimenter, and accomplished photographer and author. In this new book, he moves away from wild foods toward wildcrafted herbs and medicinal plants. *The Wildcrafting Brewer* is a book for the novice because it is mostly free of jargon related to brewing and fermenting that can impede the creative process. Instead, Baudar focuses on taste, flavor, and experimentation. He boldly suggests what flavor combinations and recipes work, as well as what flavor combinations to avoid.

Baudar implores the reader to be creative and work with his or her own flavor muse, and emphasizes that the basic process is difficult to mess up. In his introduction, he states: "If there is an overall message I want to convey, it is that brewing is fun, adventurous and extremely rewarding. Don't be afraid to experiment: You might make a few mistakes here and there, mostly in the beginning, but those will be dwarfed by the countless yummy drinks you'll create and be successful at making." True to his word, Baudar takes readers on a journey into the primitive past, when the differentiation between beer, ale, wine, and mead blurred. Baudar takes us to a time when mead and wine-making were part of the ritual of gathering and a natural expression of the individual and community.

Baudar begins with a passionate introduction to discovering and experimenting with nature's simple ingredients. He then gives a general overview of brewing; however, this is not a detailed "how to brew" book by any means. Baudar's brewing methods come from the folk method. Although the recipes are exact, the ingredients can be changed or substituted. For a reader who is new to brewing and fermenting, this book is a good starting point, but he or she may want to read a more technical brewing book for the finer points of the process. *The Wildcrafting Brewer* is 80% inspiration and exploration and 20% technique. Those readers with a background in home brewing will learn new recipes and old techniques. The equipment needed for wildcrafting brewing is basic and easily found in most kitchens.

In the chapter "Quest for Flavors," Baudar has organized herbs used for beers into five categories. Category one is the trinity of flavor herbs from old recipes: yarrow (*Achillea millefolium*, Asteraceae), bog myrtle (*Myrica gale*, Myricaceae), and mugwort (*Artemisia vulgaris*, Asteraceae). Category two is a long list of bitter and aromatic herbs that can be used together, such as horehound (*Marrubium vulgare*, Lamiaceae), wormwood (*Artemisia absinthium*), and heather (*Calluna vulgaris*, Ericaceae). Here, other references may be needed for additional details about the herbs. Category three covers the flavor herbs, fruits, and berries, and categories four and five include more bitter and obscure herbs.

The five categories are a bit arbitrary but give the beginner a simple guide, which is helpful when fermenting or brewing. In total, Baudar suggests more than 60 herbs, barks, fruits, and seeds to use in brewing. Many of the herbs are common, such as dandelion (*Taraxacum officinale*, Asteraceae), hops (*Humulus lupulus*, Cannabaceae), ginger (*Zingiber officinale*, Zingiberaceae), and basil (*Ocimum basilicum*, Lamiaceae), but others are more unique. Baudar, who lives in Los Angeles, has a great fondness for southern California plants like pinyon pine (*Pinus monophylla*, Pinaceae), prickly pear (*Opuntia* spp., Cactaceae), manzanita (*Arctostaphylos* spp., Ericaceae), and yerba santa (*Eriodictyon californicum*, Boraginaceae). I love his use of local plants, and that his own experience, excitement, and flavor combinations really come through. Who knew that green pinyon pine cones are a good source of wild yeast? Baudar always recommends that the reader find local resources to help identify plants and use general guidelines to wild harvest plants, which he calls "hardcore research."

My favorite way to use Baudar's *The Wildcrafting Brewer* is to thumb through it, look at the amazing pictures, search for appealing combinations, and then read the recipes. Most recipes have detailed pictures of the plants and the process, so it is helpful for the beginner. The pictures have a timeless, old-school, and elegant feeling that adds to the spirit of the book. It feels as if I am on an herb walk with the author having just picked the herbs for fermentation. Baudar's passion for food, herbs, and fermentation has given us a wonderful window into the ancient and modern, the scientist and folk healer.

In *The Wildcrafting Brewer,* the reader will be hard-pressed not to get excited about making wild fermentations with local herbs. To that end, Baudar has succeeded in getting the reader outside, spending time with plants, and being creative. Baudar is the ultimate wildcrafter and teacher, blending his knowledge and enthusiasm without preaching to readers. I highly recommend brewing up a ginger beer or nettle beer and starting your own wild-herb fermentation. HG

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Managing the Wild: Stories of People and Plants and Tropical Forests by Charles M. Peters. New Haven, CT and London, UK: New York Botanical Garden and Yale University Press; 2018. Hardcover, 208 pages. $30.00.



Managing the Wild is a remarkable and wonderful book that I could not put down. In fact, this is probably one of the most profound books on the interrelationships among people, plants, and tropical forest ecosystems that I have ever had the pleasure to read. The author, Charles Peters, PhD, is a field ecologist and ethnobiologist who shares some of the lessons he has learned from 35 years of field research all over the world. *Managing the Wild* presents insights that Peters learned about the sustainable management of forest resources in 15 specific locations where he conducted field work, including in Mexico, Amazonia (Peru and Brazil), West Kalimantan, Laos, Cambodia, Vietnam, China, Myanmar, Papua New Guinea, and Uganda.

Each of the 15 chapters is written in understated and easily understood prose so that anyone can access Peters' wisdom and knowledge. He is a highly respected international expert on methods to sustainably manage forest resources, and he has published numerous technical papers that document his research (including "Sustainable Harvest of Wild Plant Populations," which appeared in *HerbalGram* issue 118). In this book, he has, in many ways, become a conduit for people living in tropical forests who manage natural resources to sustain their families and communities and harvest the fruits, palm products, lumber, and rattan that are part of the local, regional, national, and international economies. Readers learn that pressures from market forces can lead to over-harvesting of natural resources, but this can be managed by measuring the production capacity of any given resource within these complex ecosystems.

In almost every location where Peters has worked, the local and indigenous people have actively managed their ecosystems at the biological, ecological, and social levels for hundreds, if not thousands, of years. Readers come to understand that local communities usually are quite interested in learning the inventory and production assessment techniques that he shares with them to ensure the long-term viability of the natural resources that the communities rely on for their well-being. He teaches the reader that "local people know a lot about managing tropical forests, and they are much better at it than we are." In fact, when the author teaches inventory techniques to community members who have a strong interest in the sustainable management of plant resources, he often returns after a period of months and finds that they have been extremely effective, completing their work swiftly and with great enthusiasm and accuracy.

At least one black-and-white photograph of a person, plant, or product accompanies each of the 15 chapters. I wish there were more photographs, as each image does speak a thousand words, but that might be appropriate for another book. For each chapter, the text also includes notes that provide full species names, explanations of forestry terminology, and citations for some of the many scientific publications that Peters and his colleagues have produced over the past 35 years.

One of the other delightful elements of this book and these stories is the deep affection the author has for the people with whom he has had the good fortune to work. He describes people in remote locations providing gracious hospitality, laughter, and human warmth to him and his colleagues. This clearly reflects how open, receptive, and aware Peters is as a scientist, field researcher, and person. This also helps explain how he comes to understand the sophisticated management systems of landscapes and resources that have been and still are implemented by local and indigenous peoples. The author learns by asking questions, spending time with elders, and looking carefully at the composition and complexity of humans and their ecosystems.

I learned that Western-trained forestry specialists often are unable to understand the way these communities are managing their natural resources. Peters provides an example that occurred in Indonesian Borneo. There, he asked a well-trained national agronomist what he thought of the carefully managed forests called *tembawang* that are created by the Dayak people. These Dayak communities and families plant and actively manage a wide diversity of species, up to 125 species per hectare, in tembawang forests. These intensively managed forest orchards look wild and uncultivated to the untrained eye. The agronomic specialist had no idea what Peters was referring to, as he did not see or understand the human-managed forests and all the foods, medicines, and other materials that they provided for the community.

The stories in this book can and hopefully will open doors of awareness for conservation organizations, environmental foundations that fund the creation of protected areas, government officials working on long-term management plans, young students eager to work on studies of sustainable harvesting, and consumers who may yearn to learn about how people really produce and manage the plants that are part of the next wave of natural health products.

I am grateful that Peters has shared these stories in a voice and rhythm that is so clear and delightful. Bravo to him for his work, this book, and his spirit. He closes this wonderful series of stories with a clear message: "At this juncture of global climate change, accelerating species extinctions, and burgeoning human populations, we must together find better ways to manage tropical forests than to degrade them or cut them down. Based on over thirty-five years of fieldwork, I am convinced that the best suggestions will come from the people who live in the forest." HG

—Steven R. King, PhD
EVP, Sustainable Supply, Ethnobotanical Research & IP
Jaguar Heath, San Francisco, California

Peter Gail
1939–2018



Peter Gail, PhD, the self-styled "King of Dandelions," died on February 14, 2018. A lifelong interest in wild and foraged foods became the foundation of Gail's career to promote the benefits of backyard weeds in the diet, specifically dandelion (*Taraxacum officinale*, Asteraceae).

Gail's knowledge of wild foods began at the age of nine, following his father's death in 1948. Struggling to make ends meet, Gail's mother learned about the prevalence of lamb's quarters (*Chenopodium album*, Amaranthaceae) in the area where they lived in southern California. Gail's mother sent him and his brother Michael out every day to forage for lamb's quarters and other wild foods, which sustained the family until his mother found a steady job. Later, in his teenage years, Gail worked at a logging camp in northern California and supplemented his diet by foraging in the woods with his friends.

After earning a bachelor's degree in biology with a botany focus from California Polytechnic State University, Gail continued to pursue his interest in botany with a master's degree in botany and plant biology from Claremont Graduate University and a doctorate in botany from Rutgers University. His primary research focus involved studying how various indigenous cultures used wild plants for food and medicine. After earning his doctorate, he was an associate professor at Cleveland State University, where he taught economic botany and environmental studies from 1972 to 1988.

A tour through Europe and interviews with local citizens in England, Belgium, and Italy showed Gail that people in the United States lacked the overall knowledge and use of wild foods that many in Europe still held. During his years of teaching, he collected local recipes that used wild foods in an effort to preserve and disseminate this knowledge.

In a 2011 interview with herbalist Susun Weed, Gail said that by 1979, he had amassed, in his estimation, the "largest collection of recipes and folklore of wild plants in the country," but that his collection "lacked organization."[1] After analyzing his collection with the intention of publishing a book, he discovered that he had more than 600 recipes for dandelion from 43 countries. Gail narrowed his focus to dandelion, which became his "flagship plant," and he began to edit and publish dandelion recipe collections in order to "help people become aware of the incredible value of this plant."

"What are 'wild foods?'" Gail asked Weed rhetorically.[1] "Americans are surrounded by vegetables going to waste." In 1988, Gail left Cleveland State University and founded the Goosefoot Acres Center for Resourceful Living in Cleveland, Ohio. Under the auspices of Goosefoot Acres, Gail devoted himself entirely to teaching and demonstrating the healthful benefits of weeds as food and medicine. He published multiple books, mostly about dandelions but also about the uses of daylilies (*Hemerocallis* spp., Asphodelaceae) and mulberries (*Morus* spp., Moraceae), among other foods. He also published "The Defenders of Dandelion" newsletter. In 1994, he founded the National Dandelion Cookoff, which ran for 10 years. Participants were invited to submit recipes to Gail; each year, he received 60-80 submissions and picked 20 finalists. His recipe collection expanded to more than 1,000 dandelion recipes from 66 different countries.

Also in 1994, Gail began producing and marketing a coffee alternative called DandyBlend, which used roasted dandelion root, roasted beet (*Beta vulgaris*, Amaranthaceae) root, roasted chicory (*Cichorium intybus*, Asteraceae) root, roasted rye (*Secale cereale*, Poaceae), and roasted barley (*Hordeum vulgare*, Poaceae) to create a healthful, caffeine-free beverage. His efforts to introduce wild foods to the diets and medicine cabinets of the United States earned him induction into the National Wild Foods Hall of Fame, part of the Nature Wonder Weekend held annually at North Bend State Park in Cairo, West Virginia, in 2000. He also appeared on multiple television programs to promote dandelions, including segments on "Good Morning America," "The Home Show," the Food Network, and Cleveland's local morning show "Morning Exchanges."

In his personal life, Gail was an active member of his church and served in leadership roles in his congregation. Congregants remembered his charity work, sense of humor, and the understanding and comfort he provided. A memorial service that celebrated the life of Peter Gail was held on February 21, 2018, in Medina, Ohio. He is survived by Wilma Gail, his wife of 57 years; his brother Michael Gail; children Karin (Dominic) Reale, Kevin (Kirsten) Gail, and Kori (Christopher) Russell; and six grandchildren. HG

—Hannah Bauman

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Christopher Hedley 1946–2017



Christopher Hedley, FNIMH, British medical herbalist and teacher of herbal medicine, died in September 2017 at the age of 71. Hedley was the oldest of three brothers, born just after World War II and raised in Kent, England. His mother loved to garden and his father was an engineering lecturer and keen nature photographer. Hedley remembered being called to plants for the first time at a young age.

In 1965, Hedley attended Sussex University to study math and physics. There, he met Non Shaw, who was studying art. They married and were together for the rest of their lives, living in the same flat near Primrose Hill in northwest London. After teaching in secondary schools, Hedley studied herbal medicine at the UK School of Phytotherapy near Tunbridge Wells beginning in the late 1970s. Non studied the course material alongside him. His relationship with Non was as central to his being an herbalist as his relationship with plants, and he credited her in everything he published.

Hedley joined the National Institute of Medical Herbalists (NIMH) in 1983, when it was still a professional body of physiomedical practitioners, many of whom had been taught by A.W. Priest. He joined the Postgraduate Training Board in 1993 and served as its chair from 1994 to 1996. He was a NIMH council member from 1993 to 1996 and was made a fellow in 1999. He was a lecturer at the Scottish School of Herbal Medicine from 1996 to 2010 and at Westminster University from 1999 to 2009. He taught materia medica, therapeutics, and pharmacy. He also taught many seminars for practitioners. Along with Non, he published *Herbal Remedies: A Practical Beginner's Guide to Making Effective Remedies in the Kitchen* (Parragon Book Service, 1996). He was also a regular contributor to the *European Journal of Herbal Medicine*.

I was lucky enough to know Christopher for 23 years. I first met him when I went to an herbal medicine evening class in the basement of Neal's Yard Remedies in Notting Hill. Each week, we did a tea tasting, then talked about the herb, its history, actions, phytochemistry, and different approaches to health care. He told wonderful stories and listened with his ears and heart wide open to all of ours.

As Christopher used to say, "Herbalism is about stories: people's stories they tell you and yours as you listen and think about how to treat them." Indeed, his stories were most likely responsible for many people deciding to study herbal medicine. Many of us owe our professions to Christopher.

"How a plant is in the world is how it will be in you," Christopher would say. "Very generous things, plants. We don't deserve them, really." Along with Non, he developed a simple-yet-sophisticated tea-tasting methodology that he used with students and practitioners, arguing that differences of opinion about an herb could almost always be resolved by taking it as a tea.

On herb walks, he would point out a particular plant and say, "And here we have the most beautiful plant in the whole known universe," before moving on to the next plant: "And here we have the most beautiful plant in the whole known universe." He loved plants. His awe and love of green nature, combined with his willingness to truly listen and his knowledge about people and plants meant that his practice thrived. Despite never having a website or advertising, he developed a loyal client base.

"When with patients, look closely and listen closely: they will tell you what's wrong with them; listen longer and they'll tell you what to do about it," he would say. "And then they pay you! It helps if you have white hair and look deeply into their eyes; they will think that you are wise!" While humor was a central part of his teaching, he was certainly wise, although he never claimed to have access to knowledge that anyone else couldn't cultivate. Christopher pointed out that the herbs we need are often under our noses, growing between the cracks in the pavement. He was an urban herbalist, and saw the city as offering up as many possibilities as meadows. He knew his patch like no one else.

People used to ask me how old Christopher was and I would reply that he was something between four and 400. He had the curiosity and twinkle of a four-year-old and the wisdom of the ancients. Non died in July 2017. Christopher followed her just after the autumn equinox. He always did have good timing.

His funeral was a wonderful affair, with about 150 people celebrating his life. There were bright smiles and tears, enough of both to make a rainbow, upon which Christopher no doubt sat and smiled, gently nodding his head. HG

—Guy Waddell, PhD, MNIMH
Medical Herbalist, Tonic Studio
London, United Kingdom

Giovanni Maciocia
1945–2018



Traditional Chinese medicine (TCM) expert and practitioner Giovanni Maciocia died on March 9, 2018, after a long illness. Maciocia was a highly respected professor and author who brought TCM practice to greater prominence throughout Europe and the United States. He was born in 1945, in Naples, Italy, and was the youngest of four children.

After earning a four-year business degree with a focus on accounting, Maciocia left Italy to travel around Europe, where he spent much time in Finland. Around 1968, he arrived in London and got a job in the accounting department at Fiat UK. Around this time, he was trying to find relief from his chronic migraines. By chance, he met a woman who suggested he try acupuncture. He was so impressed with the experience that, coupled with his interest in Chinese philosophy, he was inspired to start reading the few French books about acupuncture that existed then. In 1971, he embarked on a three-year course at the home of Diedericus van Buren, who, in 1974, founded the International College of Oriental Medicine in West Sussex.

These were very early days for acupuncturists in the United Kingdom, with only two elementary books available in English: one by Felix Mann and a book of acupuncture points by Wu Wei-Ping. They were considered precious to students in the '70s and generated enthusiasm about this system of medicine, which was largely unknown in the West.

Starting in 1974, Maciocia taught my first through third years of acupuncture and TCM, and he had a rare talent for imparting his knowledge clearly and concisely to his students. The college considered my note-taking to be exemplary, so my notes of his lectures became part of the college source material. Those notes were photocopied and sold around the world; such was the demand for information on Chinese medicine in English.

Maciocia had many interests, and he pursued them with huge devotion. In the early '70s, he became interested in early American folk music, especially blues great Huddie Ledbetter ("Lead Belly"). He taught himself to read music, then play the guitar and piano, becoming proficient at both. When he started teaching acupuncture, he realized the need to learn Chinese in order to expand his knowledge. Within two years, he became proficient in the language, adding to his fluency in English, Italian, French, Finnish, and, later, Spanish.

Maciocia was blessed with a photographic memory and studied extensively from the Chinese classics. Eventually, he developed an encyclopedic knowledge of TCM, which he later was able to impart to his students. He learned tai chi, which he practiced daily for many years, and later became an instructor. Maciocia also had an interest in Western herbal medicine, so he took the National Institute of Medical Herbalists course and qualified in 1977. He traveled to China in 1980, 1982, and 1987 to complete postgraduate courses in acupuncture and Chinese herbal medicine at the Nanjing University of Traditional Chinese Medicine. He worked with eminent physicians there, earned numerous certificates, and later was appointed Honorary Associate Professor at the university. He also completed a two-year course in Chinese herbal medicine with Ted Kaptchuk, DOM, in the mid-'80s in the United States.

In 1987, Maciocia launched the first school of Chinese herbal medicine in London with Michael McIntyre. He then created a range of Chinese herbal formulas designed to treat common Western ailments. His line of "Three Treasures," "Women's Treasures," and "Little Treasures" pills comprise 91 different formulae. He recognized the need for more comprehensive books on Chinese medicine, so he turned his attention to writing some of the most highly regarded textbooks on various aspects of TCM. Over a period of 28 years, he wrote seven books in total, as well as five new editions of the originals, and they have been translated into 10 languages.

Maciocia loved opera and knew many arias by heart. Beethoven was another passion of his, especially the Third Symphony because it "broke all the rules." He was also very keen on English football, or "soccer." He admitted his two heroes were Kenny Dalglish (a footballer) and Sun Simiao (a famous Chinese doctor from the Tang dynasty). This exemplifies Maciocia's diverse character.

His passion for Latin American music led him to learn salsa dancing in the last decade of his life. He continued to dance during his illness, and was famous for hosting the best salsa parties in Santa Barbara, California, complete with mariachi bands, fire dancers, and *taqueros*. In the months before his death, he became interested in the history of World War II, and read great tomes on the subject. His thirst for knowledge was insatiable throughout his life. His greatest gift was his generosity in sharing his knowledge with others, particularly his students of Chinese medicine. He did this by lecturing worldwide, hosting webinars, creating numerous online courses, giving clinical tips on social media, making videos, and writing articles and books.

The world has lost a great mind and an inspirational teacher. I am extremely grateful to have been one of his students and a close friend for 45 years. HG

—Linda Upton
Member, British Acupuncture Council
Member, Register of Chinese Herbal Medicine
Cheltenham, United Kingdom


Photo ©2018 Young Living

Donald Gary Young
1949–2018

Donald Gary Young, founder of Utah-based Young Living Essential Oils, died on May 12, 2018, at the age of 68 following a series of strokes. Young founded the company to provide essential oils and natural products to consumers, and he eschewed retail stores in favor of the multi-level marketing model to reach millions of customers in the United States and around the world. What began with the purchase of 160 acres in Idaho in 1989 is now a billion-dollar enterprise with, according to Young Living's website, more than four million local and international members.

Young was born in Idaho Falls, Idaho, on July 11, 1949. After graduating high school in 1967, he moved to British Columbia, Canada, and was granted a homestead for logging and ranching. In 1973, he suffered an injury in the course of his work and was told that he would never walk again. This experience drove him to explore alternative treatment options, and he eventually learned about the therapeutic use of essential oils at a conference in Geneva, Switzerland. He spent 13 years re-learning how to walk, and the next several decades studying the art of distillation and the science behind essential oils.

According to the Young Living website, Young's education included practical training in nutrition and naturopathy from Bernadean University; biochemistry and anatomy in Mexico; the effects of essential oils on the respiratory system with Jean-Claude Lapraz, MD; essential oil chemistry with Radwan Farag, PhD; gas chromatography at Anadolu University in Eskisehir, Turkey; and essential oil distillation with Henri Viaud and Marcel Espieu in France. Equipped with this information, he opened his first essential oil business in 1988 in Spokane, Washington, which would eventually pave the way for the creation of Young Living.

Young continued to develop and refine his distillation techniques, as he reportedly was dissatisfied with the quality of essential oils available in the US market at the time. Following the purchase of 160 acres in St. Maries, Idaho, he cultivated lavender (*Lavandula* spp., Lamiaceae), clary sage (*Salvia sclarea*, Lamiaceae), thyme (*Thymus vulgaris*, Lamiaceae), and peppermint (*Mentha* × *piperita*, Lamiaceae) for this use. In 1993, he developed a proprietary process for essential oil distillation, and, in 1994, he and his wife Mary founded Young Living Essential Oils.

As the company expanded, Young sought to either grow the raw materials necessary for the production of essential oils or procure them from reputable sources. He acquired more land in Idaho and Utah, and the company purchased its first international production site in 2006 in Guayaquil, Ecuador. In Ecuador, Young discovered a new mission for himself and his company: philanthropy. He observed the poor condition of the school attended by local children in the village of Chongon, near Young Living's farm, and decided to build a modern facility and hire professional educators. The Young Living Academy opened in late 2006, achieved a 100% graduation rate, and inspired the founding of Young's charity, The D. Gary Young, Young Living Foundation, in 2009.

Meanwhile, Young continued to innovate and seek out sources of raw materials. In 2010, Young Living opened a distillery in Salalah, Oman, to process and distill frankincense (*Boswellia* spp., Burseraceae) and myrrh (*Commiphora myrrha*, Burseraceae). In 2014, the Young Living Highland Flats distillery in Naples, Idaho, opened and, according to the company, was the first automated, large-capacity, computerized steam-distillation facility for essential oils in the world. Young was recognized by *Direct Selling News* with its inaugural BRAVO Legacy Award in 2018 for his contributions to the direct selling community.

The D. Gary Young, Young Living Foundation continued to carry out Young's philanthropic missions of empowerment, wellness, and education, partnering with organizations in Cambodia and Uganda to reach underserved children and combat human trafficking, childhood poverty, and the spread of malaria. The Young Living Foundation also pursued its own initiatives, which included rebuilding efforts in Yarsa, Nepal, following devastating earthquakes in April 2015. The project began in 2016 and finished in April 2018, culminating in the construction of the Young Living Academy, Yarsa Primary School. To raise awareness and funds for the effort, Young participated in two dogsled races in Alaska. The Young Living Foundation maintains a disaster relief fund for members impacted by natural disasters.

At the time of Young's death, he served as chairman of the board of Young Living Essential Oils. The company has announced that Mary Young, his wife, will continue to serve as the company's chief executive officer.[1] Young is survived by Mary and their two sons, Jacob and Josef. HG

—Hannah Bauman

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Photo taken by John Cummings with a Sony DSC W330 camera and a Vario-Tessar lens.

American Ginseng
Panax quinquefolius, Araliaceae

American ginseng (*Panax quinquefolius*, Araliaceae) is an herbaceous perennial native to midwestern and northeastern North America.[1] Preparations of the root and whole plant were used medicinally in some indigenous American traditions, such as the Cherokee and Iroquois.[2] Following exportation to China in the early 18th century, the root also was used in traditional Chinese medicine (TCM). In TCM, American ginseng is considered a cooling tonic for the respiratory and digestive systems.[3]

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