HerbalGram 129 • Feb – April 2021

Yerba Maté Herb Profile • Herbal Supply Chain Update • ABC Launches New Website
Thailand Approves Andrographis for COVID-19 • Elder Berry & Viral Infections Review

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dear *reader*

My friend and colleague Mark Plotkin once asked me, "What is the most widely used botanical medicine?" I immediately answered, "garlic." It seemed a reasonable answer, and it was on my mind at the time because I was preparing a keynote speech on the history of garlic for the International Garlic Symposium in Japan. "No," he said, "It's wine!" We discussed his reasons and agreed that this topic would make an interesting article.

Now, his richly illustrated "Ethnobotany of Wine" cover story explores the origins and history of wine in Transcaucasia, Mesopotamia, the Mediterranean, and beyond. Plotkin is an ethnobotanist and author known mainly for his laudable work with indigenous peoples in the Amazon via his nonprofit Amazon Conservation Team (his new book, *The Amazon: What Everyone Needs to Know*, is reviewed on pages 72-74). He also wrote "Notes on the Ethnobotany of Warfare" in *HerbalGram* issue 101, which includes a section about wine. I'm not certain that wine is actually more widely used as a medicine than garlic, but I definitely prefer it as a beverage.

In my kitchen is a small, hollow gourd, the curved top of which is used as a handle, with a hollow metal tube (*bombilla*) about six inches long. I purchased this from a roadside vendor on the cross-Andes highway from Santiago, Chile, to Mendoza, Argentina. For centuries, vessels like this have been used to drink yerba maté tea. Yerba maté, which is in the same genus as guayusa and yaupon, has been the primary caffeinated beverage of a large area of South America, particularly Argentina and neighboring countries, where it is consumed more than coffee. No longer limited to South America, beverages from the dried or roasted leaves of this member of the holly family have become increasingly popular in many parts of the world in the past decades. In this issue, regular contributors Josef Brinckmann and Thomas Brendler provide a comprehensive profile on this traditional stimulant.

Political changes, weather conditions, and other factors are known to impact supply, availability, and prices of culinary, medicinal, and aromatic plants sold in international commerce. In 2020, a global pandemic became one of these factors. In this issue, frequent contributor Karen Raterman provides a second article about how the COVID-19 pandemic is affecting the global supply chain for various medicinal plants. Her previous article on this topic was published in issue 126. For this update, Raterman interviewed more than a dozen spokespeople from the herb industry, and they share their companies' experiences, measures taken, and lessons learned during the pandemic.

Of considerable international interest is that, in December 2020, the Thai government approved andrographis leaf extract for the treatment of COVID-19 symptoms after documenting positive results in preliminary studies, as noted in *HerbalGram* Assistant Editor Connor Yearsley's article. Andrographis is known for its beneficial effects in upper respiratory infections, and it will be interesting to see if future research confirms its potential benefits for COVID-19 and whether other countries follow suit.

ABC Special Projects Director Gayle Engels, who has worked at ABC for more than 25 years, reports on the organization's new website, which has been in development for more than two years, and the progression of the website since 1995. Gayle has been the primary steward of ABC's efforts to upgrade and enhance its extensive and content-rich site, which has more than 62,500 distinct pages in 11 resource sections of research and educational content.

Also, we honor the lives of two people dedicated to the study and rational use of medicinal plants: our dear friends of many years, Professor Walter Lewis and Bill Keller, who made significant contributions to the ethnobotany and pharmacognosy communities.

Finally, in 2020, ABC and the Sustainable Herbs Program (SHP) initiated a series of educational webinars on the resource-rich SHP Sustainability & Regenerative Practices Toolkit, ethnobotany, and individual herbs in commerce. SHP Director Ann Armbrecht leads these compelling and inspiring conversations with prominent ethnobotanists, industry representatives, and others. We are deeply grateful that thousands of people in dozens of countries have viewed the webinars, which indicates that ABC and the herbal community are global entities. The webinar series and other ABC accomplishments and activities are described in the year-in-review article in this issue. HG

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departments

On the Cover
Bacchus oil painting (ca. 1598) by Caravaggio. Artwork courtesy of Le Gallerie Degli Uffizi, Italy.

Contributors

Marilyn Barrett, PhD
Thomas Brendler
Josef Brinckmann
Mariann Garner-Wizard
Edward J. Kennelly, PhD
A. Douglas Kinghorn, PhD, DSc
Roger Mustalish, PhD
Heather S. Oliff, PhD
Jenny Perez
Mark Plotkin, PhD, LHD
Karen Raterman
Samaara Robbins
Eric Yarnell, ND, RH(AHG)

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For information about Small Business or Sponsor Memberships, contact Denise Meikel at denise@herbalgram.org or 512-926-4900.

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***HerbalGram* Staff**

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Sahar Hanrahan
Advertising Sales
512-926-4900 ext. 129
sahar@herbalgram.org
advertising@herbalgram.org

Yerba maté
Ilex paraguariensis
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Yerba Maté

Ilex paraguariensis
Family: Aquifoliaceae

By Josef Brinckmann and Thomas Brendler

INTRODUCTION

Ilex paraguariensis, commonly known as yerba maté, is one of 500 to 600 species in the genus *Ilex*,[1] which belongs to the holly family (Aquifoliaceae) of shrubs and trees.[2] *Ilex* species are distributed in tropical and subtropical to temperate regions, mainly in tropical Central and South America.[2] An understory tree that occurs in mixed *Araucaria angustifolia* (Araucariaceae) forests in South America, *I. paraguariensis* is native to Argentina, Bolivia, Brazil, Paraguay, and Uruguay.[3]

The tree thrives at elevations between 1,000 and 2,000 feet (304.8 and 609.6 m) in alluvial or humus-rich soils.[4] *Ilex paraguariensis* trees are functionally dioecious (male and female flowers occur on separate plants) and, in natural forest conditions, can reach up to 35 meters (114.8 feet) tall,[5] although some authors report an upper height of 16 meters (52.5 feet).[6] On plantations and smaller family farms, the trees are pruned and may be kept at 12 to 30 feet (3.7 to 9.1 m) tall.[7] *Ilex paraguariensis* is a long-lived understory tree, and populations of hundreds of individual trees per hectare are found in mountainous subtropical forests of northeastern Argentina, southern Brazil, and Paraguay.[5] However, cattle grazing in *Araucaria* forest ecoregions is one of the main factors reducing the density of *I. paraguariensis* trees and modifying their distribution pattern.[8]

Ilex paraguariensis is cultivated on about 326,000 hectares (805,564 acres) in Argentina, Brazil, and Paraguay, and an estimated 1 million metric tons (MT) of leaves are harvested each year. Argentina accounts for about 85% of global production,[9] which is not to be confused with global export trade volume. Most of the harvest remains in South

America, where yerba maté is consumed in an estimated 98% of Argentinian households. Another source reports that yerba maté is consumed in more than 90% of households in Argentina, Paraguay, and Uruguay, and the economies of entire provinces are heavily dependent on yerba maté production and trade.[10]

In 2019, about 80,332 MT of yerba maté leaf were exported from South America.[11] The top three exporters, accounting for most of the supply in terms of volume were Argentina (39,698 MT), Brazil (36,203 MT), and Paraguay (4,196 MT). In recent years, drinking yerba maté tea has spread to Arab countries, with Syria being a main importer from Argentina (Jorge Alonso, president of the Latin American Society of Phytomedicine, email to T. Smith, January 26, 2021). The United States imported 7,615 MT of yerba maté leaf in 2019, mainly from Argentina and Brazil, with smaller amounts from Ecuador, Paraguay, and Uruguay.[12]

HISTORY AND CULTURAL SIGNIFICANCE

In his 1737 work *Genera Plantarum*, Swedish botanist Carl Linnaeus (1707-1778) assigned the genus name *Ilex*,[13] which was already used in the Latin name for the Mediterranean holly oak (*Quercus ilex*, Fagaceae), probably due to the similar glossy leaves.[14] The species name *Ilex paraguariensis*, referring to Paraguay, was given by French botanist Auguste François César Prouvençal de Saint-Hilaire (1779-1853) in his account of a six-year journey (1816-1822) through the interior of Brazil and to Paraguayan missions, which he presented at the French Academy of Sciences (Paris, France) and published in the 1822 ninth volume of *Mémoires du Muséum d'Histoire Naturelle*.[15] Saint-Hilaire described three varieties of *I. paraguariensis*: *obtusifolia*, *acutifolia*, and *angustifolia*.[16]

Ilex paraguariensis is listed among the economic plants encountered by English biologist and naturalist Charles Darwin (1809-1882) on his five-year voyage around the world on the *HMS Beagle*. While in Argentina and Chile, Darwin drank yerba maté tea as a substitute for tea (*Camellia sinensis*, Theaceae). In a letter sent from Buenos Aires to his sister in England, Darwin wrote: "I am become quite a Gaucho; drink my Mattee and smoke my cigar."[17]

Ilex paraguariensis, whose leaves are used to prepare the herbal tea called *chimarrão* or *maté*, is a cultural keystone species of indigenous peoples of Argentina, Brazil, Paraguay, and Uruguay. Traditional knowledge of production, processing, and consumption of yerba maté has been passed to each generation since pre-colonial times.[18] *Yerba* is a Spanish word that means "herb." *Maté* is reportedly a Quechua word that is associated with the terms *cabaca* (gourd) or *cuia* (dried gourd used as a cup). The name maté has come to mean the contents of the *cuia*, namely the herbal tea infusion of the leaves of *I. paraguariensis* prepared in the *cuia*.[16]

According to Williams (1962):

> The traditional utensils for drinking maté are the *cuia* and *bombilla*. The *cuia* is usually a dried, often decorated, gourd with a round apical opening two or three inches in diameter. The *bombilla*, a hollow metal tube, has a bulb-like or spoon-shaped strainer at the lower end, through which the beverage is sipped. To prepare the infusion the *cuia* is half filled with ground maté leaves, over which boiling water is poured.[4]

Possibly the earliest archaeological evidence of human use of yerba maté was detected in plant micro remains from a pipe found at Catamarca in northwestern Argentina, dated to the Lower Formative Period (650 BCE–500 CE). Carbonized leaves of yerba maté, coca (*Erythroxylum coca*, Erythroxylaceae), lemon verbena (*Aloysia citrodora*, Verbenaceae), and tobacco (*Nicotiana* spp., Solanaceae) were identified.[19] Similar administration of yerba maté by aspiration (inhalation) among the Tehuelche people of Patagonia is reported in ethnographic literature.[20] Tupí-Guaraní-speaking peoples were already managing yerba maté production in tropical rainforests at the time of first contact with Europeans around 1500. Non-indigenous use of yerba maté and commercial trade spread via Jesuit missionaries.[21]

After the Spanish conquest of Paraguay, three colonies were established (in 1554, 1557, and 1576) expressly for the purpose of harvesting yerba maté leaves using enslaved Guaraní people for labor. After 1578, Jesuit priests gradually took control over the yerba maté industry despite its exploitation of indigenous people.[16] After the end of the War of the Triple Alliance (1864–1870), with Paraguay defeated by the alliance (Argentina, Empire of Brazil, and Uruguay), "recruitment" of indigenous Guaraní-Kaiowás farm workers increased. A few large-scale transnational corporations dominated yerba maté production and trade in the last decades of the 19th century, using semi-enslaved indigenous farm labor from the defeated Paraguayan territories.[22]

In Brazil, *espinheira-santa* (*Maytenus ilicifolia*, Celastraceae) leaf is traditionally mixed with yerba maté leaf in the preparation of *maté* or *chimarrão* to counteract known minor side effects, such as heartburn and stomach pain, experienced by some people when drinking yerba maté as a single herb tea infusion.[23] (The same traditional combination is used in Paraguay but not known to be used in Argentina [Jorge Alonso, email to T. Smith, January 26, 2021].) Yerba maté branches, leaves, and stems are used by the Yungas people of northwestern Argentina as a source of green dye prepared with mordants (dye fixatives) including alum, urine, salt, and vinegar.[24]

In Argentinian ethnomedicine, the aerial parts of yerba maté reportedly are used for galactagogue (promotes lactation) and cicatrizant (promotes wound healing by forming scar tissue) actions, while herbal tea infusions of the leaf are used for treating conditions related to influenza and for scurf (dandruff).[25] A yerba maté monograph was included in the first edition of the *Farmacopea Argentina* in 1898, omitted from the second edition in 1921,[26] readmitted into the seventh edition in 2002,[27] and remains official in

the currently valid eighth edition. The first edition of the *Farmacopéia Brasileira*, published in 1929, included a yerba maté monograph. However, it was omitted from the second edition, published in 1959.

A quality standards monograph for yerba maté entered the 1948 supplement to the sixth edition of the *German Pharmacopoeia* (Folia Mate DAB Erg.-B.6).[28] However, the monograph was not retained in the seventh edition(s) of the pharmacopeias of the former West Germany (DAB 7 1968) and former East Germany (DAB 7-DDR 1973). Two monographs entered the German Drug Codex (DAC) in 1986: cured and roasted maté leaf (Mate folium tostum) and green maté leaf (Maté folium viride).[29] In 1988, the German Commission E published a positive therapeutic monograph for yerba maté (*Maté folium — Mateblätter*), prepared as powdered leaf for oral ingestion or as cut leaf for making an herbal tea infusion, indicated for treating mental and physical fatigue.[30]

In 2010, the European Food Safety Authority (EFSA) issued an opinion that a cause-and-effect relationship had not been established between the consumption of yerba maté and a beneficial physiological effect related to an increase in renal water elimination (diuresis).[31] Also in 2010, the European Medicines Agency (EMA) published a labeling standards monograph for Mate folium that superseded the German Commission E monograph for purposes of product marketing authorization in the European Union.[32] However, in 2018, an official quality standards monograph entered the fourth supplement to the ninth edition of the *European Pharmacopoeia* (PhEur 9.4),[33] which superseded the national monographs of France and Germany for purposes of a marketing authorization holder establishing quality specifications for yerba maté leaf, if used as an active ingredient of a registered traditional herbal medicinal product (THMP) in the European Union (EU).

CURRENT AUTHORIZED USES IN COSMETICS, FOODS, AND MEDICINES

In the United States, yerba maté is marketed as a beverage tea for energy, similar to caffeine-containing leaves of other *Ilex* species such as guayusa (*I. guayusa*) and yaupon (*I. vomitoria*). The US Food and Drug Administration (FDA) classifies natural extractives of yerba maté as generally recognized as safe (GRAS) for use in conventional food products.[34] It may also be used as a component of dietary supplement products, which require notification with the FDA within 30 days of marketing if a structure-function claim is made.[35] In its 2003 final rule on ingredient labeling of dietary supplements that contain botanicals, the FDA used yerba maté as an example of a non-English herb name that could be used as the standardized common name on product labeling.[36]

In Canada, yerba maté is regulated as a medicinal ingredient of licensed natural health products (NHPs), which require pre-marketing authorization from the Natural and Non-prescription Health Products Directorate (NNHPD). Licensed NHPs containing yerba maté extract equivalent to six grams dried leaf (not exceeding 150 mg caffeine per day) may carry claim statements to the effect of "helps temporarily to promote alertness and wakefulness, and to enhance cognitive performance," "helps temporarily to relieve fatigue," and/or "helps temporarily to support mental sharpness."[37]

In the EU, cut, dried yerba maté leaf may be used as an active ingredient of registered THMPs, for preparation as an herbal tea infusion, and labeled with the therapeutic indications "for symptoms of fatigue and sensation of weakness" and/or "to increase the amount of urine to achieve flushing of the urinary tract as an adjuvant in minor urinary complaints."[32] The dried leaf used for production of registered THMPs must conform to the quality standards monograph of the *European Pharmacopoeia*.[38] However, it may also be marketed as a food beverage (without claims) in some Member States because it was in the EU market as a food or food ingredient and consumed to a significant degree before May 15, 1997. This means that its access to the EU market is not subject to the Novel Food Regulation. *Ilex paraguariensis* also appears on the Belgian list of plants that are considered to be not novel for use in food supplements and herbal teas.[39] Furthermore, use of an extract of the leaves in cosmetic products in the EU is authorized specifically for hair-conditioning, perfuming, and skin-conditioning functions.[40]

MODERN RESEARCH

The primary active compounds in yerba maté leaves include polyphenols, xanthines, saponins, and caffeic acid derivatives, which have demonstrated antimicrobial, antioxidant, antidiabetic, cardioprotective, and metabolic effects in multiple pre-clinical investigations.[41-44] Clinical research has focused on applications of yerba maté in metabolic disorders, including weight management,[45-47] metabolic syndrome,[48] and diabetes,[49] but also exercise performance and for cardiovascular benefits,[44,50-52] as detailed in Table 1.[53-76]

Outcomes of safety assessments of yerba maté in multiple pre-clinical and clinical settings are heterogeneous and controversial. A yerba maté dry extract showed no acute or 90-day subchronic toxicity in rats and rabbits at 2 g/kg body weight.[77] An aqueous extract showed no signs of reproductive toxicity in rats.[78] A cross-sectional study in 5,304 pregnant women, 68% of whom habitually consumed yerba maté, showed no association with prematurity, intrauterine growth, or duration of pregnancy.[79]

Carcinogenicity has been attributed to high levels of polycyclic aromatic hydrocarbons (PAHs) in yerba maté.[80,81] Furthermore, consumption of hot yerba maté was associated with increased risk of cancer of esophagus, larynx, and oral cavity in several epidemiological studies.[81-84] However, breast cancer risk was found to be inversely associated with yerba maté consumption in a study assessing 572 cancer

Table 1. Clinical Trials with Preparations of Yerba Maté

Publication	Study Design	Interventions	Outcomes
Alkhatib (2014)[53]	RCT, 14 healthy fasted males and females (7/7)	1 g ground leaves or placebo on two occasions, followed by 60 min rest and subsequent 3-minute incremental cycling exercise	Fatty acid oxidation (FAO) and energy expenditure derived from FAO significantly increased during exercise in maté group, without affecting peak oxygen uptake and blood lactate concentration.
Alkhatib & Atcheson (2017)[54]	RCT, 12 healthy fasted females (6/6)	2 g ground leaves or placebo on two occasions, followed by 120 min rest and subsequent 30-minute cycling exercise	FAO, Profile of Mood States (POMS) score, and subjective appetite scale (visual analog scale; VAS) were measured at baseline and during exercise. FAO and POMS scores were significantly higher, while VAS scores were significantly reduced vs. placebo during exercise.
Areta et al (2017)[55]	Crossover RCT, 11 trained cyclists	Maté leaf and stem (5 g) or placebo for 5 days before trial, 1-2 weeks washout between trials	Incremental cycling test measuring maximum oxygen consumption (VO_2 max) was performed at baseline 2 weeks before trial sessions. Blood samples were taken before and during exercise. Submaximal step-test and time trials (TT) were performed on ergometers. Respiratory gases were measured. Maté increased resting plasma adrenaline concentration and fat utilization and improved TT performance.
Avena et al (2019)[56]	Three-arm OS, 119 overweight women	Maté + restricted diet, maté alone, or water + restricted diet for 12 weeks	Anthropometric measurements, total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, and triglycerides were examined at baseline and after completion. Total cholesterol decreased significantly in all groups, LDL significantly decreased in both maté groups and HDL in maté only, triglycerides significantly decreased in the maté + diet group.
Balsan et al (2019)[57]	Three-arm RCT, 142 (47/49/46) overweight men and women	Maté (175 g), green tea (5 g), or apple tea (5 g) in 1 L of hot water for 8 weeks	Serum levels of leptin and paraoxonase-1 (PON-1) were examined at baseline, 4, and 8 weeks. PON-1 and HDL significantly increased in the maté group and also intergroup.
Becker et al (2019)[58]	OS, 14 healthy subjects	Spray-dried maté aqueous extract, 2,250 mg daily for 60 days	Maté significantly increased serum antioxidant capacity, reduced glutathione (GSH), superoxide dismutase (SOD), catalase (CAT), and PON-1 activities, and decreased lipid hydroperoxides (LOOH) and thiobarbituric acid reactive substance levels.
Boaventura et al (2015)[59]	Three-arm, crossover RCT, 31 healthy subjects	Traditional maté infusion, freeze-concentrated maté, or water, one treatment each with a 2-week washout period between	Antioxidant enzyme activities, CAT, SOD, glutathione peroxidase (GPx), GSH, lipid peroxidation (LOOH), and antioxidant capacity of serum were measured before and 60 min after treatment. CAT, SOD, GPx, GSH, and serum antioxidant capacity increased significantly with maté concentrate, while traditional maté only increased GSH.
Celestino et al (2017)[60]	Crossover RCT, 17 overweight women	Three tablets of herbal combination (112 mg maté, 95 mg guarana [*Paullinia cupana*, Sapindaceae], and 36 mg damiana [*Turnera diffusa*, Passifloraceae] standardized extracts) or placebo, with a 7-day washout	Blood samples were taken at baseline and at specific time points within a 7-hour period during which controlled food intake (breakfast and lunch) occurred. After breakfast, glucagon-like peptide 1 (GLP-1) concentration was significantly higher with maté combination, energy intake and acylated ghrelin were significantly reduced at and after lunch, respectively.
Conforti et al (2012)[61]	146 postmenopausal women	Not applicable	Correlation of maté consumption with bone mineral density (BMD). Consumption of > 1 L of maté per day was associated with significantly higher lumbar spine and femoral neck BMD.
Cuesta et al (2018)[62]	OS, 50 habitual maté drinkers with cardiovascular risk factors	Holter monitor (portable electrocardiogram) at baseline and after 24 days without maté consumption	No significant changes in heart rate or arrhythmia incidence rate were observed.
da Silva et al (2008)[63]	OS, 12 healthy fasted subjects	500 mL maté infusion	In blood samples collected before and one hour after intake, plasma and LDL oxidation, plasma antioxidant capacity, and platelet aggregation were monitored. Lipid peroxidation was significantly inhibited, presence of oxysterols decreased in plasma, and LDL and plasma antioxidant capacity increased significantly, while platelet aggregation remained unaffected.
da Veiga et al (2018)[64]	95 postmenopausal women	Not applicable	Correlation of maté consumption with incidence of cardiovascular risk factors. Consumption of > 1 L of maté per day was associated with significantly lower risks for coronary disease, dyslipidemia, and hypertension.

Table 1 (continued). Clinical Trials with Preparations of Yerba Maté

Publication	Study Design	Interventions	Outcomes
de Morais et al (2009)[65]	RCT, 102 (15 normolipidemic, 57 dyslipidemic, 30 hypercholesterolemic on statin therapy) subjects	1 L maté (50 mg or 20 mg/mL green or roasted, respectively) daily for 40 days	Blood samples were collected at -30, -15, 0, 20, and 40 days. LDL was lowered significantly in all subjects. In dyslipidemic subjects, apolipoprotein B was significantly reduced and HDL increased. Triglyceride levels were unchanged.
Gatto et al (2015)[66]	223 subjects with Parkinson's disease (PD), 406 controls	Not applicable	Correlation of maté consumption with incidence of PD. Consumption of maté was found to be inversely associated with incidence of PD.
Jung & Hur (2016)[67]	RCT, 33 (17/16) obese women	3,000 mg/day maté extract or placebo for 6 weeks	Body weight (BW), composition, body mass index (BMI), waist circumference (WC), and safety parameters were monitored at baseline, 3, and 6 weeks. While BW and BMI did not change significantly, trunk fat percentage significantly decreased with maté.
Kim et al (2012)[68]	RCT, 60 (30/30) overweight subjects	3,000 mg/day green maté extract or placebo for 6 weeks	BW, composition, BMI, WC, and safety parameters were monitored at baseline and 6 weeks. A significantly greater reduction in body fat and fat mass was observed with maté.
Kim et al (2015)[69]	RCT, 30 (15/15) obese subjects	3,000 mg/day maté extract or placebo for 12 weeks	Abdominal fat distribution, anthropometric parameters, blood lipid profiles, and safety parameters were monitored. Body fat percent and mass and waist-hip ratio decreased significantly with maté. No clinically relevant changes occurred in the safety parameters.
Klein et al (2011)[70]	RCT, 58 (29/29) type-2 diabetic and pre-diabetic subjects	Maté tea (1 L with 20 g maté leaves) (11/11), maté + nutrition counseling (9/10), or nutrition counseling only (9/8) for 60 days	Blood samples were taken at baseline, 20, 40, and 60 days. Maté consumption improved glycemic control and lipid profile of type-2 diabetic subjects and combined with nutritional intervention significantly decreased serum lipid parameters of pre-diabetic individuals.
Maufrais et al (2018)[71]	RCT, 23 healthy subjects	3.4 g of instant unsweetened maté tea, 500 mL cold or hot, single dose	Heart rate, skin blood flow, hand temperature, baroreflex sensitivity, fat oxidation, and energy expenditure were measured at baseline and 90 min. Cold tea induced greater stimulation of thermogenesis and fat oxidation.
Messina et al (2015)[72]	OS, 121 dyslipidemic subjects	50 or 100 g maté daily for 12 weeks	TC, LDL, triglycerides, atherogenic index (AI), and body composition were monitored. TC and LDL decreased significantly in both groups, triglycerides only in the 50 g group. AI did not change significantly.
Panza et al (2016)[73]	Crossover RCT, 12 (7/5) healthy subjects	Instant maté tea, 1 g in 200 mL cold water or control for 11 days, with a 17-day washout	Subjects performed eccentric exercise protocol with one arm. Maximal isometric force of elbow flexor muscles was measured before, at 0, 24, 48, and 72 h after exercise. Blood samples were obtained before and at 24, 48, and 72 h after exercise and analyzed for total phenolics, GSH, glutathione disulfide (GSSG), GSH:GSSG ratio, and LOOH. Maté significantly improved the rate of strength recovery. GSH decreased in control but not with maté. No other significant changes were observed.
Ribeiro et al (2017)[74]	OS, 8 (4/4) patients with severe traumatic brain injury	7 g (300 mL) of maté twice daily or no treatment for 14 days	Between-group glycemia levels differed non-significantly. However, treated subjects showed better glycemic profile and needed less insulin. Treatment group showed significant decrease in serum creatine phosphokinase.
Souza et al (2017)[75]	Crossover RCT, 92 HIV/AIDS patients on antiretroviral therapy	3 g maté tea, maté placebo (no polyphenols) or 65 g of chocolate, or chocolate placebo (no polyphenols) for 15 days, with 15-day washout	Lipid profiles were determined at baseline and after each intervention. Only chocolate significantly increased HDL. Maté consumption did not result in significant alterations in the lipid profile.
Yu et al (2015)[76]	RCT, 142 (71/71) volunteers with high blood viscosity	1,500 mL of maté tea (commercial product) or placebo for 6 weeks	Nailfold microcirculation assessment and hemorheological measurements including serum 6-keto-PGF1α and thromboxane B2 (TXB2) assays were taken at baseline and after 6 weeks. With maté, whole blood viscosity, plasma viscosity, and Equation K value of erythrocyte sedimentation rate (ESRK) decreased significantly, blood flow speeds accelerated, and nailfold weighted integral values significantly decreased, 6-keto-PGF1α increased, and TXB2 decreased.

OS: Observational study RCT: Randomized, controlled trial

cases and 889 controls.[85,86] One case report associates yerba maté consumption with veno-occlusive disease of the liver; however, causality is questionable.[87] A more reliable causal link between yerba maté consumption and acute hepatitis is reported in another case report.[88]

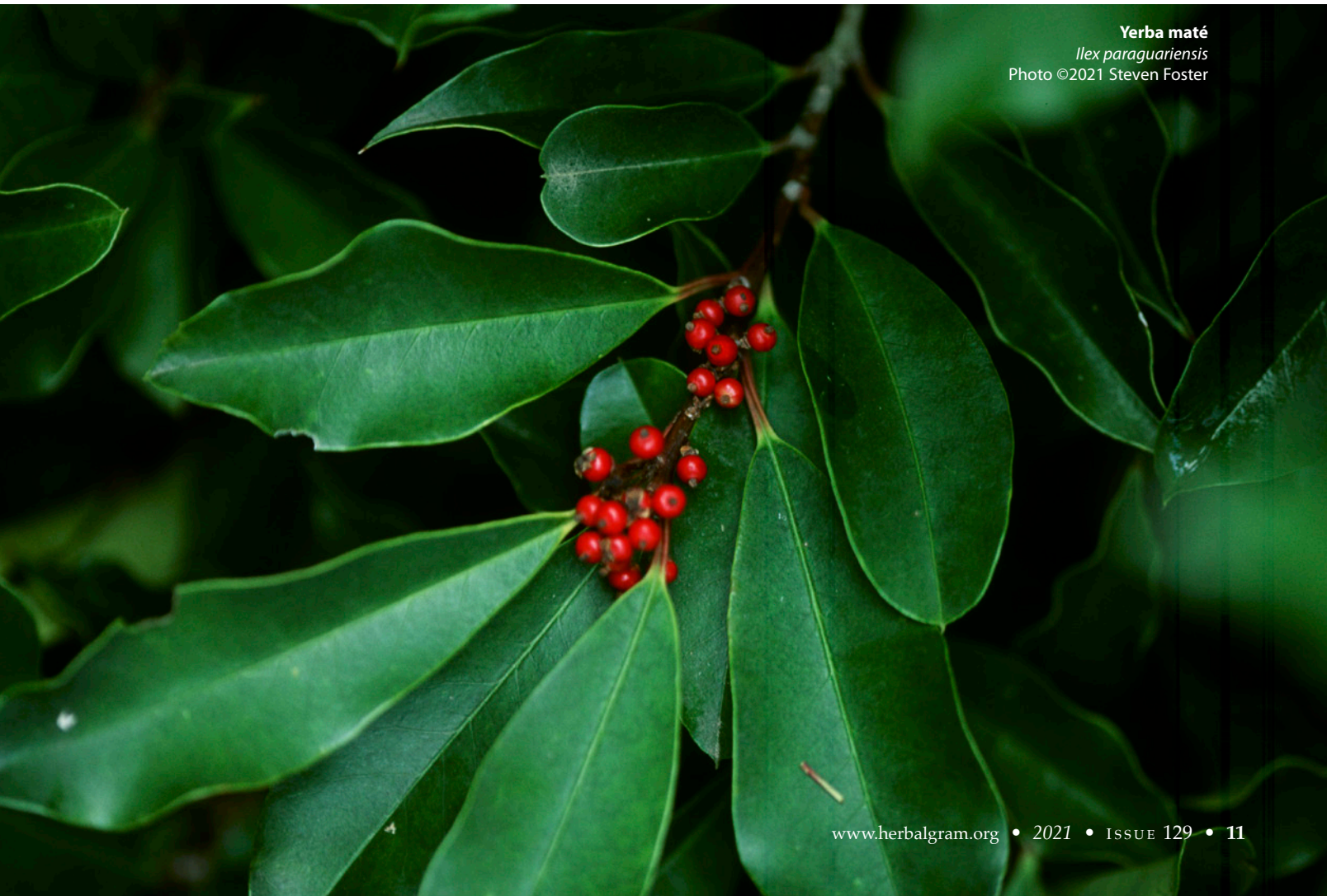
ADULTERATION

Other *Ilex* species have similar traditional uses and have been reported as adulterants of yerba maté.[89] Confusion with the leaves of other *Ilex* species in wild collection have included *I. dumosa* and *I. theezans*, but also leaves of cassava (*Manihot esculenta*, Euphorbiaceae) and juçara (*Euterpe edulis*, Arecaceae).[90] In Brazil, local congeneric substitutes or adulterants of *I. paraguariensis* reportedly have included *I. argentina*, *I. brevicuspis*, *I. dumosa* var. *dumosa*, *I. integerrima*, *I. microdonta*, *I. pseudobuxus*, *I. taubertiana*, and *I. theezans*.[91] *Ilex paraguariensis*, but not all *Ilex* species (e.g., *I. brevicuspis*), contains methylxanthines; therefore, the absence of these compounds would indicate that *I. paraguariensis* is not present in a tested sample (Jorge Alonso, email to T. Smith, January 26, 2021).

The *European Pharmacopoeia* monograph for testing of yerba maté (Mate Folium PhEur 10)[38] provides macroscopic, microscopic, thin-layer-chromatography (TLC), and high-performance-liquid-chromatography (HPLC) tests for confirming composition, identity, quality, and strength. Furthermore, the labeling standards monograph of the EMA requires, in addition to compliance with a pharmacopeial monograph for quality, adequate control of the PAH content in yerba maté leaf.[32] In the EMA's 2016 reflection paper on PAHs in herbal medicinal products, the agency stated that very high concentrations of PAHs have been detected in yerba maté leaves, and in both hot and cold infusions. PAHs are created when substances such as coal, oil, gas, and organic waste are burned incompletely. According to the EMA: "This can arise due to contamination by environmental sources, as the lipophilic properties of these compounds allow their adsorption onto atmospheric particles and direct deposition in sediments, soils and plants, or during the post-harvest processing."[92] The yerba maté industry is reportedly making progress on strategies for managing and lowering PAH content.

SUSTAINABILITY AND FUTURE OUTLOOK

The International Union for Conservation of Nature (IUCN) assigned wild *I. paraguariensis* to the conservation category of near threatened (NT),[3] meaning the species is close to the threatened thresholds or would be threatened without ongoing conservation measures. However, the assessment was published in 1998 and may need updating.



Yerba maté
Ilex paraguariensis
Photo ©2021 Steven Foster

A project for biodiversity conservation and sustainable land management implemented by the United Nations Development Programme (UNDP) focusing in the Upper Paraná Atlantic Forest (UPAF), which includes a large part of Paraguay's Eastern Region, included sustainable yerba maté production in its scope.[93] One project outcome was the planned implementation and promotion of sustainable yerba maté production under agroforestry systems (AFS). The plantations are to be established specifically in areas aiming to restore protective forests of water channels.[94]

One Argentinian study reported that yerba maté as a monoculture causes erosion and soil exhaustion and, therefore, recommended establishment and management of certified organic yerba maté in AFS. Organic yerba maté in AFS along with certain native trees can improve soil fertility without use of fertilizers and increase farmer income. Several native tree species recommended in the study for AFS intercropping with yerba maté include *Araucaria angustifolia*, *Cordia trichotoma* (Boraginaceae), *Nectandra lanceolata* (Lauraceae), *Ocotea puberula* (Lauraceae), and *Tabebuia heptaphylla* (Bignoniaceae), among others.[6]

In the 21st century, a considerable global market for sustainably produced yerba maté emerged and continues to grow. An increasing number of export-oriented yerba maté farming and processing operations in South America have implemented voluntary sustainability standards such as the Demeter Biodynamic Farm and Processing Standards, Ecocert Fair for Life Standards, Fairtrade International (FLO) fair trade standards, Fair Trade USA Agricultural Production Standards, and United States Department of Agriculture (USDA) Organic Standards.

For example, the farm Triunfo do Brasil Ltda (Paraná, Brazil), founded in 1925, harvests yerba maté in an organic-certified natural forest area of 2,000 hectares that is also Fair for Life and Fair Trade USA certified.[95] There are Demeter Biodynamic certified yerba maté farms such as Matebrás Indústria do Mate Ltda ME in Brazil and Guayakí Latin America SA Reserva Agroecológica Iguazú in Argentina, the latter of which is also Fair for Life certified.[96] Guayakí (Sebastopol, California) also has an organic- and Fair for Life-certified producer in Brazil (Guayakí Yerba Mate Brasil Produção e Comércio LTDA). Other Fair for Life-certified yerba maté operations in Brazil include Cooperativa de Reforma Agrária e Erva-Mate (COPERMATE), Ervateira Catanduvas, Industría de Erva Mate Yacuy Ltda, NAT'Organico Produtos Naturais, and Qualitá Brasil Mate & Chá, among others.[97]

There are also FLO fair trade-certified yerba maté operations in Brazil including Associação dos Produtores Ecológicos do Centro-Sul do Paraná and the aforementioned NAT'Organico.[98] There is an evident healthy global market for sustainable yerba maté, produced according to credible standards for ecological, economic, and social sustainability. HG

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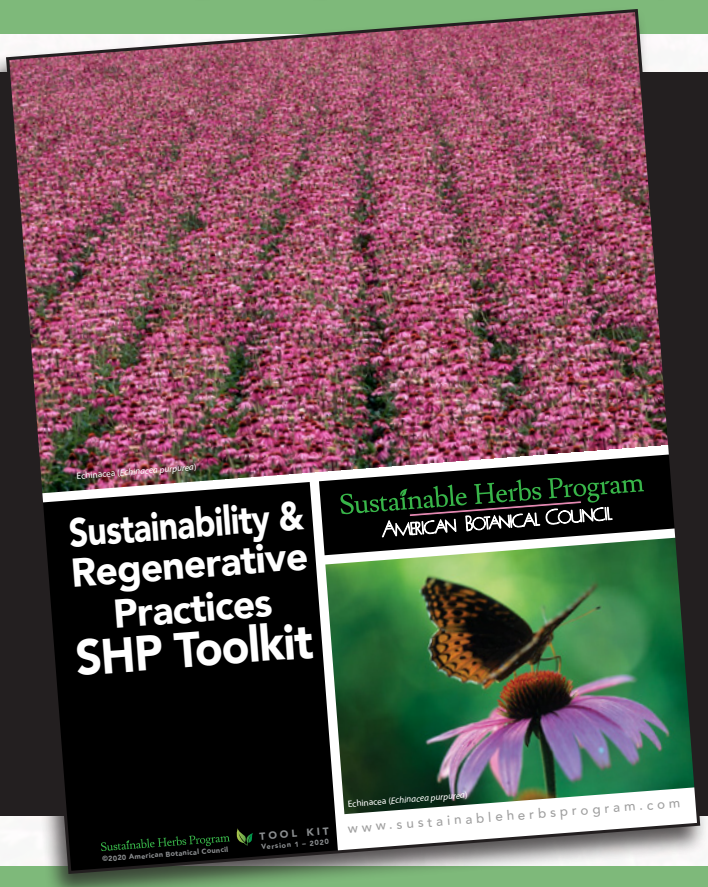

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The American Botanical Council's Adopt-an-Herb Program provides a mutually beneficial opportunity to support ABC's nonprofit educational efforts and promote a company's most important herbs.

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

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

Parties interested in taking part in the Adopt-an-Herb Program are invited to contact ABC Development Director Denise Meikel at 512-926-4900, extension 120, or by email at denise@herbalgram.org.

AMERICAN BOTANICAL COUNCIL
SINCE 1988

Herbal Adopters

iff Health	**Oat** *Avena sativa*
eUROMED	**Milk Thistle** *Silybum marianum*
	Fig *Ficus carica*
CENTROFLORA NUTRA Now part of Givaudan	**Yerba Maté** *Ilex paraguariensis*
Nature's Gift	**Helichrysum** *Helichrysum italicum*
PHARMACTIVE BIOTECH PRODUCTS	**Saffron** *Crocus sativus*
EMBRIA Health Sciences	**EpiCor® Fermentate** *Saccharomyces cerevisiae*
JIAHERB essentials of nature	**Rhodiola** *Rhodiola rosea*
neem BIOTECH A ZALUVIDA COMPANY.	**Garlic** *Allium sativum*
	Artichoke *Cynara cardunculus* Scolymus Group
DMH ingredients	**Baobab** *Adansonia digitata*
	Rooibos *Aspalathus linearis*
BEEHIVE BOTANICALS	**Propolis**
YOUR LOGO	**Plant name** *Scientific name*

NEW ADOPTER!

Bionutricia Extract • Power of plant •	**Asian Holly Oak** *Quercus infectoria*
KD Authentic Botanical Extracts	**Senna** *Senna alexandrina*
Soladox BOTANICALS	**Black Chokeberry** *Aronia melanocarpa*
	Elderberry *Sambucus nigra*
	Stinging Nettle *Urtica dioica*
natural Factors	**Echinacea** *Echinacea* spp.
Pharmatoka	**Cranberry** *Vaccinium macrocarpon*
FOUR ELEMENTS	**Lemon Balm** *Melissa officinalis*
BRASSICA	**Broccoli** *Brassica oleracea* Broccoli Group
DownUnder enterprises	**Tea Tree** *Melaleuca alternifolia*
Aromatics INCORPORATED	**Peppermint** *Mentha x piperita*
HERBALIFE	**Aloe Vera** *Aloe vera*
Symphony NATURAL HEALTH	**Maca** *Lepidium meyenii*
Terry Naturally EuroPharma	**Turmeric** *Curcuma longa*

Visit us at www.herbalgram.org/adopt

Contact Denise Meikel at 512-926-4900 x120
or by email at denise@herbalgram.org

Herbal Adopters

layn USA	**Japanese Sophora** *Styphnolobium japonicum*
	Monk Fruit *Siraitia grosvenorii*
PLT Health Solutions — Growth through Innovation	**Indian Frankincense** *Boswellia serrata*
Loomis® Enzymes	**Rose Hip** *Rosa canina*
Ginseng Plus®	**Notoginseng** *Panax notoginseng*
Far Long®	**Lifeflower** *Erigeron breviscapus*
Botalys — Better plants for a better life	**Asian Ginseng** *Panax ginseng*
NAHA	**Lavender** *Lavandula angustifolia*
Verdure Sciences®	**Pomegranate** *Punica granatum*
KSM-66®	**Ashwagandha** *Withania somnifera*
RFI — From Field to Formula	**Hibiscus** *Hibiscus sabdariffa*
SFI™	**Bacopa** *Bacopa monnieri*
Nature's Way®	**Ginkgo** *Ginkgo biloba*
biotropics Malaysia	**Kesum** *Persicaria minor*
	Tongkat Ali *Eurycoma longifolia*
Diana — Performance from nature — Food	**Acerola** *Malpighia spp.*
Contains Zembrin®	**Sceletium** *Sceletium tortuosum*
pukka	**Shatavari** *Asparagus racemosus*
natural™ Remedies	**Andrographis** *Andrographis paniculata*
	Licorice *Glycyrrhiza spp.*
Artemis International	**Tart Cherry** *Prunus cerasus*
	Black Currant *Ribes nigrum*
	Purple Corn *Zea mays*
Brauer natural medicine	**Chamomile** *Matricaria chamomilla*
grownetwork™	**Rough Horsetail** *Equisetum hyemale*
valensa	**Saw Palmetto** *Serenoa repens*
Naturopathica® Holistic Health	**Arnica** *Arnica montana*
Future Ceuticals	**Coffee Fruit** *Coffea spp.*
Teawolf — Natural Extract Solutions	**Guayusa** *Ilex guayusa*
Gaia Trading Company, Inc.	**Hops** *Humulus lupulus*
The Actives Factory	**Birch** *Betula spp.*
Natac — Science to Market	**Olive** *Olea europaea*
	Grape *Vitis vinifera*
Ecoso Dynamics	**Devil's Claw** *Harpagophytum spp.*

Become an adopter today!

ABC Celebrates Gayle Engels' 25th Anniversary with the Organization

By Hannah Bauman

When Gayle Engels started working with the American Botanical Council (ABC) as sales manager in May 1995, the nonprofit education organization was still two years away from the purchase of its headquarters and herb gardens at the historic Case Mill Homestead in Austin, Texas. At the time, the 12-person team worked out of Founder and Executive Director Mark Blumenthal's home in northwest Austin. "We had taken over so much of [Mark's home], there was no room for him to live there anymore," Engels recalled (email, December 7, 2020). "My office was in a small bedroom and, for a time, four of us shared the space."

Despite the cramped quarters, Engels strived to help ABC have an outsized effect on its stakeholders and the herbal medicine community, and her efforts contributed to the organization's growth. "All the projects ABC has seen to fruition over the years might lead people to believe that we have always worked with a bigger staff and budget than we have," she wrote. Within the first five years of working at ABC, Engels expanded the organization's catalog of books, videos, and other media to more than 600 items, including some hard-to-find and out-of-print texts. Before large online retailers like Amazon, this was an invaluable resource for ABC members.

Engels is now ABC's special projects director and oversees its website development and administration, supervises the education department and gardens, and manages other projects as needed.

Over her 25 years of service to the organization, Engels has witnessed significant changes at ABC, including the purchase of the Case Mill Homestead in 1997, the revitalization of the dietetic and pharmacy internship program, and the digitizing of publications, which began in 2001. Currently, her largest project is the complete overhaul of ABC's web presence with a new platform and website, which launched in January 2021 and has been ongoing for several years. The new website is responsive across mobile devices and has improved navigation, a full-text search engine, the ability to seamlessly connect with customer relationship management applications, and improve access to subscription content for libraries, universities, and other licensees.

In addition to her projects at ABC, Engels is also the national coordinator of HerbDay. HerbDay was founded in 2006 by a coalition of five national organizations: ABC, the American Herbalists Guild, the American Herbal Pharmacopoeia, the American Herbal Products Association, and United Plant Savers. On or around the first Saturday in May, these and other organizations, garden groups, and individuals are encouraged to hold public educational events celebrating the importance of herbs and herbalism. Engels manages the national HerbDay website, which is also currently undergoing a redesign, and Facebook page (OfficialHerbDay). She also coordinates the activities and speakers for ABC's HerbDay celebration, which is typically ABC's biggest public event. ABC cancelled its HerbDay event in 2020 due to the COVID-19 pandemic, and the 2021 celebration will go forward as a virtual event in case any safety concerns still exist.

Engels on an ABC pharmacy ecotour in the Amazon in 1998.

Before starting at ABC, Engels had experience with nursery and greenhouse management, education, and publishing in and around Austin while she worked toward a degree in secondary education from the University of Texas at Austin (UT). "While some of these jobs took me to other locations, I always gravitated back to Austin," she wrote. "And while all my jobs were interest-

ing and valid learning experiences at the time, the three things that excited me the most were learning about and working with plants (specifically herbs), education, and book and magazine publishing (everything from writing them, to the noise of the presses and smell of the ink, to promoting them)."

When a friend introduced her to ABC, Engels saw a career that fulfilled her professional goals. "I had an interview with Mark, and within ten minutes, I knew I had found a mentor and an organization that I could work with for the rest of my life," she wrote.

Blumenthal said: "Gayle is definitely an integral part of ABC's DNA. Hiring Gayle at ABC was a no-brainer. With her background managing a plant nursery, secondary education, and managing circulation, subscriptions, and sales for three magazines, she had more qualifications than we were seeking for the position for which she applied. And, she was smart and engaging! It took me only a few nanoseconds to realize that I really wanted this woman to be part of the future of ABC. After 25 years, I've never regretted that decision. She is a real asset to not only ABC, but to the entire medicinal plant community!"


Engels at the ABC Celebration in Anaheim, CA.

In 2008, Engels made the decision to relocate from Texas to Oregon, and she is grateful for the support from Blumenthal and the ABC staff in redefining her job description to allow it. Before the pandemic, she returned to the ABC campus multiple times a year, including HerbDay and the annual onsite Board of Trustees meetings, to meet with the education and gardening departments and pitch in with the gardens in person.

Engels thinks the growth of the internship program is one of her biggest accomplishments at ABC. In 2002, as education director, she began to restructure the program for graduating health care professionals. In its current format, the interns, the majority of whom are part of the pharmacy program at UT or the dietetic program at Texas State University in San Marcos, gain hands-on experience with ABC Education Coordinator Jenny Perez. They are introduced to herbs from the ground up and learn about plant propagation in the garden, plant chemistry, and the basics of medicine-making. Each intern is also responsible for a research project on an individual plant's phytochemistry.

"From the beginning, it was important to ABC leadership that the internship program expand students' awareness of the extent of reliable sources of scientific and traditional information available about herbs and phytomedicines," Engels wrote. "One of the best things I was able to do for this program was find, hire, and work with Jenny."

In 2019, Engels was honored with the inaugural Madalene Hill Award for Excellence in Herbal Education from the Herb Society of America.[1] The award reflects her commitment to education and deep knowledge of herbs and their uses, and is doubly important to Engels because Madalene Hill, known as the "Grand Dame of Herbs," was a friend and mentor to her before Hill's death in 2009.

From her home in Oregon, Engels stays busy outside of work with gardening, reading, plant walks, art journaling, sewing, cooking, and making her own herbal preparations.

Engels reflected on her professional life before joining ABC: "In the early to mid-1990s, I was putting together three lists: things I had done in previous jobs that I never wanted to do again (burned that one), things I had done in previous jobs that I wanted to continue doing, and things I had not had the opportunity to do yet." At ABC, she has found a home that continues to challenge her with new opportunities and allows her to pursue her passions. HG

Reference

1. Bauman H. ABC's Gayle Engels to Receive Inaugural Award for Excellence in Herbal Education. *HerbalGram*. 2019;121:19-20. Available at: http://cms.herbalgram.org/herbalgram/issue121/hg121-abcnews-award-gayle.html. Accessed December 10, 2020.

2020: American Botanical Council's Year in Review

ABC adapts and thrives amid pandemic, launching new webinar series and publications

By ABC Staff

Despite the challenges and uncertainty of 2020, the American Botanical Council (ABC) continued to thrive and expand its reach, launching a new webinar series, producing new publications, and finishing a multi-year effort to completely redesign and enhance its website.

The COVID-19 pandemic serves as a strong reminder of the need for science-based information, which ABC continued to disseminate in 2020 in new and enhanced ways. Reaching members in more than 80 countries, ABC delivers vital, authoritative information about the valuable role medicinal and other beneficial plants play in health care and self-care through several channels, including an information-rich website (a new and improved version was launched in January 2021), peer-reviewed publications, an expanding Botanical Adulterants Prevention Program (BAPP), the Sustainable Herbs Program (SHP), an internship program for dietetic and pharmacy students, media education, webinars, lectures, and more.

"Fortunately, we at ABC were able to assess our priorities and adapt quickly to the changing environment created by the COVID-19 pandemic," said Mark Blumenthal, ABC's founder and executive director. "I'm very pleased to say that ABC's staff rose to the challenge willingly and brilliantly, often working harder than ever, and so we were able to not only maintain our commitment to ABC's unique nonprofit research and educational mission, and the vast majority of our extensive publications and programs, but to actually expand some of our offerings."

New Webinar Series and SHP Sustainability Toolkit

During its second year as part of ABC, SHP continued to promote and inspire industry efforts toward a responsible, sustainable, and regenerative herb value network. In April, SHP published "The SHP Sustainability & Regenerative Practices Toolkit," a resource guide for botanical industry companies to assess and improve their sustainability efforts. As of December 2020, this invaluable resource had been downloaded nearly 900 times and had more than 2,000 pageviews on SHP's website.

In addition, ABC and SHP launched a new series of free, popular webinars. Originally, the webinars were focused on sustainability and the SHP toolkit. However, after positive reception, ABC expanded the series to include webinars on subjects related to ethnobotany and single medicinal herbs in commerce. To date, some of the webinars have been viewed more than 4,000 times.

Botanical Adulterants Prevention Program Updates

BAPP continued to establish itself as a leading and authoritative source of information on herbal ingredient authenticity, counterfeiting, and fraud — topics that became even more relevant during the COVID-19 pandemic. In 2020, BAPP released the revised draft of "Best Practices Standard Operating Procedure (SOP) to Prevent Resale of Irreparably Defective Articles" for a second round of industry and public comment. This included revised contract language and frequently asked questions that explained how BAPP responded to 106 comments received in the initial public comment period. The comment periods will help ensure that the documents and SOP have a wide basis of industry and public support. ABC and BAPP plan to release the finalized versions of the SOP and contract language in 2021.

Internship Program Goes Virtual

In response to COVID-19 restrictions, ABC's dietetic and pharmacy internship program, led by ABC Education Coordinator Jenny Perez, shifted to a completely online format. This involved providing virtual classes, creating educational videos, and delivering herbal medicine distance-learning kits to interns. The kits contain herb samples that interns use in virtual labs led by Perez as part of their instruction in the basics of botany, phytochemistry, and herbal preparations.

Publication Highlights

ABC published its 2019 Herb Market Report in *HerbalGram* issue 127 with, for the first time, same-year data for the first six months of 2020 that highlighted the increased sale of various immune-related herbs and medicinal fungi during the initial phase of the pandemic.

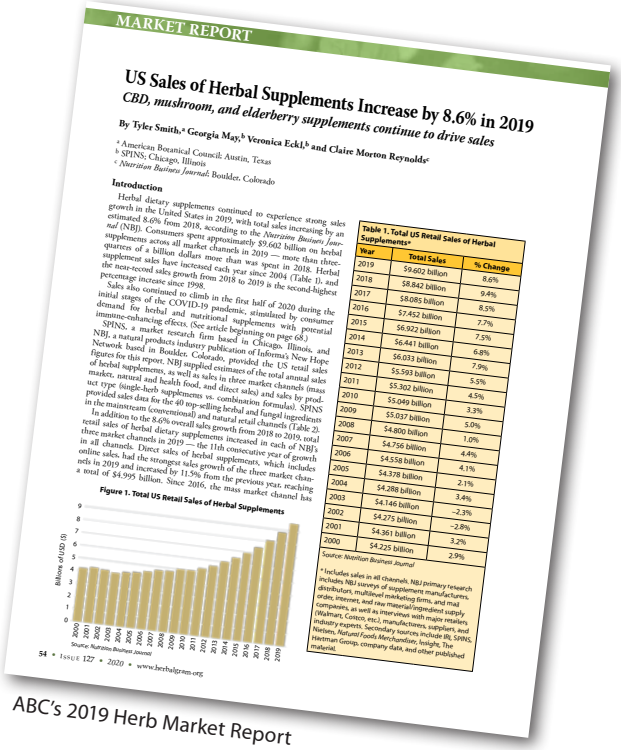
ABC's Food as Medicine initiative on the health benefits of common edible plants published its 60th article. These articles are consistently some of the most popular articles in ABC's monthly HerbalEGram electronic newsletter. In 2020, *HerbalGram* also introduced a new Food as Medicine page, which includes highlights from a recent Food as Medicine article published in HerbalEGram.

ABC Finishes Website Redesign

Throughout 2020, ABC Special Projects Director Gayle Engels continued to lead ABC's effort to modernize and enhance its website. The redesigned website went live in January 2021.

In addition, in 2020:

- BAPP published three Botanical Adulterants Prevention Bulletins, one Laboratory Guidance Document, and three Botanical Adulterants Monitor newsletters, raising the total of all BAPP peer-reviewed documents to 62.
- ABC trained four interns, introducing sixth-year pharmacy school and graduate dietetic students to the science behind botanicals and herbal medicine.
- ABC Chief Science Officer Stefan Gafner, PhD, chaired a risk assessment group during the Society for Medicinal Plant and Natural Product Research (GA) eSymposium Session in September 2020.
- Gafner also co-authored two articles in peer-reviewed scientific journals and gave eight virtual presentations, including one for SANA, the International Exhibition of Organic and Natural Products.
- ABC presented six Botanical Excellence Awards to individuals and companies for their valuable contributions to the US and global botanical community.
- The 75th herb was adopted on ABC's HerbMedPro database through the ABC Adopt-an-Herb program.
- ABC issued 21 press releases.
- ABC published four issues of *HerbalGram*, 12 issues of HerbalEGram, 51 issues of Herbal News & Events, and 384 HerbClips.
- ABC purchased a residential property immediately adjacent to its headquarters at the historic 2.5-acre Case Mill Homestead in East Austin, thereby creating expansion opportunities for ABC's nonprofit research and educational mission in the future.


MARKET REPORT

US Sales of Herbal Supplements Increase by 8.6% in 2019

CBD, mushroom, and elderberry supplements continue to drive sales

By Tyler Smith,[a] Georgia May,[b] Veronica Eckl,[b] and Claire Morton Reynolds[c]

[a] American Botanical Council; Austin, Texas
[b] SPINS, Chicago, Illinois
[c] *Nutrition Business Journal*; Boulder, Colorado

Introduction

Herbal dietary supplements continued to experience strong sales growth in the United States in 2019, with total sales increasing by an estimated 8.6% from 2018, according to the *Nutrition Business Journal* (NBJ). Consumers spent approximately $9.602 billion on herbal supplements across all market channels in 2019 — more than three-quarters of a billion dollars more than was spent in 2018. Herbal supplement sales have increased each year since 2004 (Table 1), and the next-second sales growth from 2018 to 2019 is the second-highest percentage increase since 1998.

Sales also continued to climb in the first half of 2020 during the initial stages of the COVID-19 pandemic, stimulated by consumer demand for herbal and nutritional supplements with potential immune-enhancing effects. (See article beginning on page 68.)

SPINS, a market research firm based in Chicago, Illinois, and NBJ, a natural products industry publication of Informa's New Hope Network based in Boulder, Colorado, provided the US retail sales of herbal supplements, as well as sales in three market channels (mass market, natural and health food, and direct sales) and sales by product type (single-herb supplements vs. combination formulas). SPINS provided sales data for the 40 top-selling herbal and fungal ingredients in the mainstream (conventional) and natural retail channels (Table 2).

In addition to the 8.6% overall sales growth from 2018 to 2019, total retail sales of herbal dietary supplements increased in each of NBJ's three market channels in 2019 — the 11th consecutive year of growth in all channels. Direct sales of herbal supplements, which includes online sales, had the strongest sales growth of the three market channels in 2019 and increased by 11.5% from the previous year, reaching a total of $4.995 billion. Since 2016, the mass market channel has

Figure 1. Total US Retail Sales of Herbal Supplements

Source: Nutrition Business Journal

Table 1. Total US Retail Sales of Herbal Supplements*

Year	Total Sales	% Change
2019	$9.602 billion	8.6%
2018	$8.842 billion	9.4%
2017	$8.085 billion	8.5%
2016	$7.452 billion	7.7%
2015	$6.922 billion	7.5%
2014	$6.441 billion	6.8%
2013	$6.033 billion	7.9%
2012	$5.593 billion	5.5%
2011	$5.302 billion	4.5%
2010	$5.049 billion	3.3%
2009	$5.037 billion	5.0%
2008	$4.800 billion	1.0%
2007	$4.756 billion	4.4%
2006	$4.558 billion	4.1%
2005	$4.378 billion	2.1%
2004	$4.288 billion	3.4%
2003	$4.146 billion	−2.3%
2002	$4.275 billion	−2.8%
2001	$4.361 billion	3.2%
2000	$4.225 billion	2.9%

Source: Nutrition Business Journal

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

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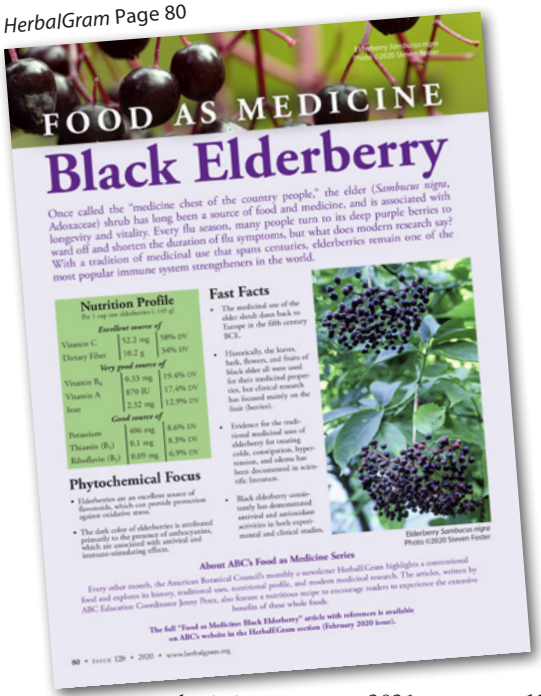
ABC's 2019 Herb Market Report

As these tangible and important accomplishments show, ABC was able to continue all but its in-person activities in 2020, despite the challenges presented by the COVID-19 pandemic. ABC is now, more than ever, being recognized worldwide as a highly credible, respected, and important source of information on the science behind herbs, herbal ingredient authenticity, and herb sustainability and conservation. HG

HerbalGram Page 80


FOOD AS MEDICINE

Black Elderberry

Once called the "medicine chest of the country people," the elder (*Sambucus nigra*, Adoxaceae) shrub has long been a source of food and medicine, and is associated with longevity and vitality. Every flu season, many people turn to its deep purple berries to ward off and shorten the duration of flu symptoms, but what does modern research say? With a tradition of medicinal use that spans centuries, elderberries remain one of the most popular immune system strengtheners in the world.

Nutrition Profile

Per 1 cup raw elderberries (~95 g)

Excellent source of		
Vitamin C	52.2 mg	58% DV
Dietary Fiber	10.2 g	34% DV
Very good source of		
Vitamin B_6	0.33 mg	19.4% DV
Vitamin A	870 IU	17.4% DV
Iron	2.32 mg	12.9% DV
Good source of		
Potassium	406 mg	8.6% DV
Thiamin (B_1)	0.1 mg	8.3% DV
Riboflavin (B_2)	0.09 mg	6.9% DV

Fast Facts

- The medicinal use of the elder shrub dates back to Europe in the fifth century BCE.
- Historically, the leaves, bark, flowers, and fruits of black elder all were used for their medicinal properties, but clinical research has focused mainly on the fruit (berries).
- Evidence for the traditional medicinal uses of elderberry for treating colds, constipation, hypertension, and edema has been documented in scientific literature.
- Black elderberry consistently has demonstrated antiviral and antioxidant activities in both experimental and clinical studies.

Phytochemical Focus

- Elderberries are an excellent source of flavonoids, which can provide protection against oxidative stress.
- The dark color of elderberries is attributed primarily to the presence of anthocyanins, which are associated with antiviral and immune-stimulating effects.

Elderberry Sambucus nigra
Photo ©2020 Steven Foster

About ABC's Food as Medicine Series

Every other month, the American Botanical Council's monthly e-newsletter HerbalEGram highlights a conventional food and explores its history, traditional uses, nutritional profile, and modern medicinal research. The articles, written by ABC Education Coordinator Jenny Perez, also feature a nutritious recipe to encourage readers to experience the extensive benefits of these whole foods.

The full "Food as Medicine Black Elderberry" article with references is available on ABC's website in the HerbalEGram section (February 2020 issue).

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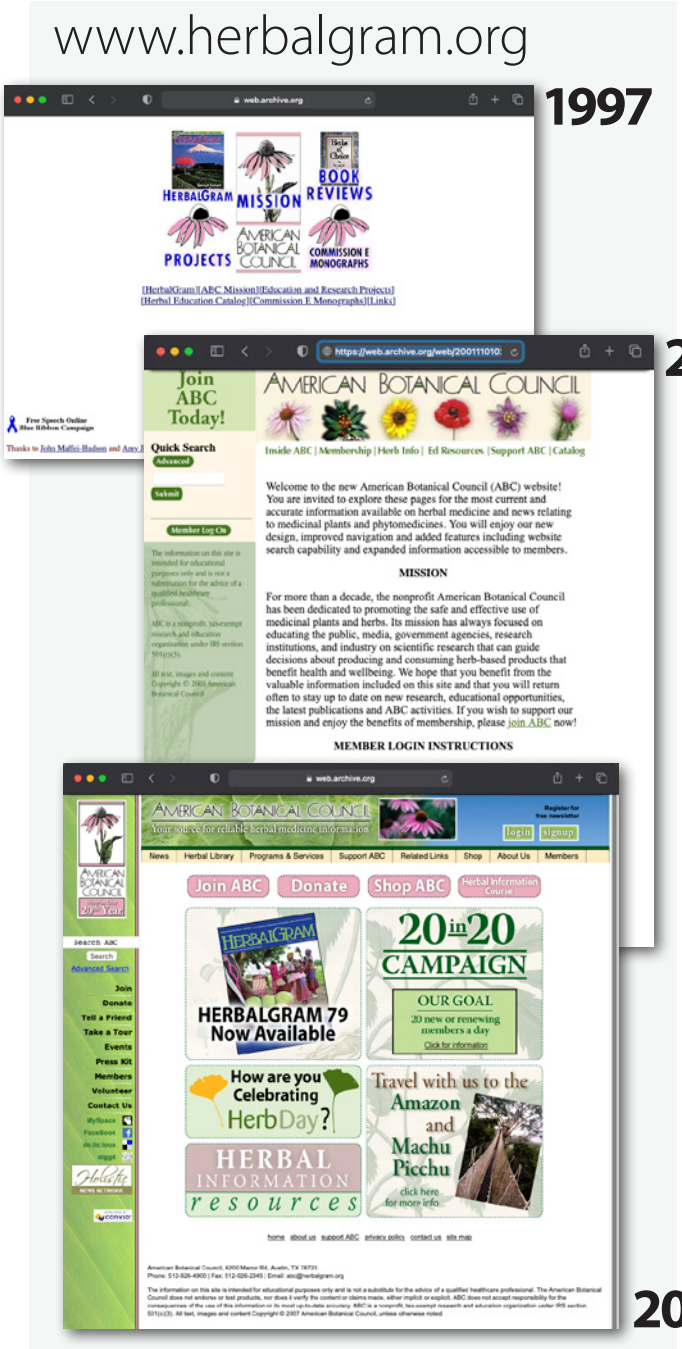
The Evolution of the American Botanical Council Website: 1995 – 2021

By Gayle Engels

In January 2021, the American Botanical Council (ABC) launched a revised and redesigned version of its website, www.herbalgram.org. The new website is mobile friendly, with improved navigation, a modern design, enhanced graphics, additional development capabilities, and a more intuitive user experience for site visitors and ABC staff who add content to the site. It has been 25 years since ABC introduced its first website, and the process of improving the site will continue for years to come as the digital landscape continues to evolve.



Then

ABC developed its first website in 1995, just two years after the European Organization for Nuclear Research (CERN) released the World Wide Web software to the public domain and announced that "the web" was free for everyone to use and develop.[1]

In the beginning, the ABC website was very basic. Users could find ABC's contact information and request additional details about books, *HerbalGram*, and ABC's ethnobotanical ecotours. The "Content" section included an *HerbalGram* page with information on legal and regulatory news, medicinal plant research, and profiles on herbs and herbalists, along with ABC's mission statement, educational and research projects, book reviews, and how to order from the ABC "Bookstore" (including "Back Packs" of past *HerbalGram* issues and indices). Online ordering was uncommon at the time, so *HerbalGram* subscriptions and the hundreds of books and other educational items in ABC's Herbal Education Catalog were available to order by phone, fax, or US mail only. Websites for organizations of ABC's size were so new and rare that an article in *HerbalGram* issue 35 gave instructions for how to access the web.

Shortly after the website launched, ABC hired a webmaster, Trey Bennett, who oversaw regular updates of content on the site, including selected herb monographs, ABC-developed accredited continuing education programs for health care professionals, links to related sites, and information about ABC's new home at the historic 2.5-acre Case Mill Homestead in Austin, Texas. In early 2000, Netscape's "Web Site Garage" had awarded "American Botanical Council Online" an Excellent Diagnosis, its highest award, for the site's browser compatibility, load time, popularity, and HTML (hypertext markup language, the standard website programming language) design, among other technical criteria.

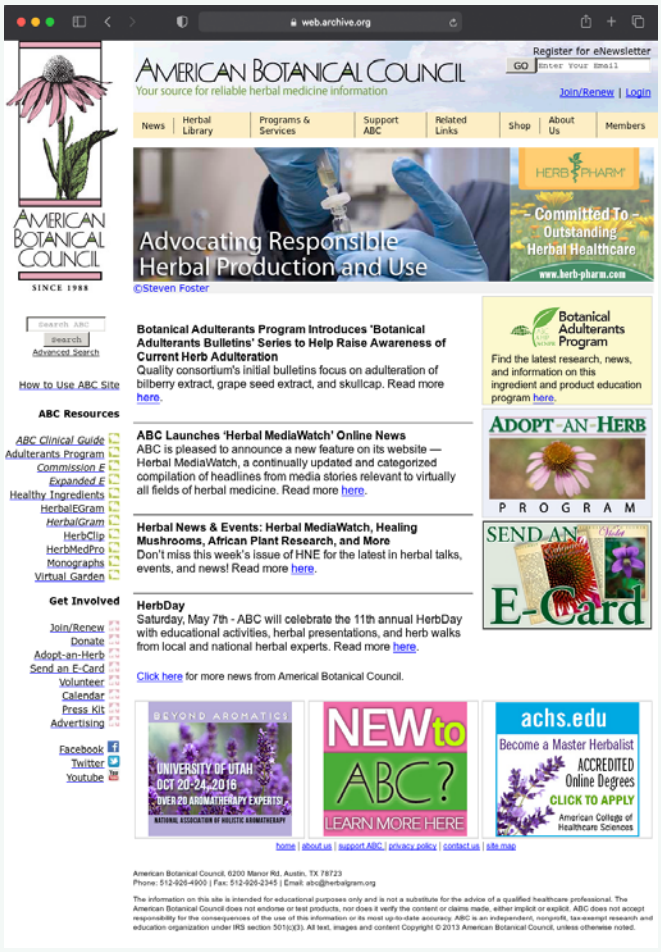
By 2000, the technology had developed so that ABC was able to offer what was then considered secure online ordering. The

complete 32-page Herbal Education Catalog was added to the website and included more than 300 books, herbal videos, software, ABC's 14 Botanical Booklets on individual herbs, third-party literature, American Herbal Pharmacopoeia monographs, special reports and publications, a CD-ROM of 102 medicinal plant photographs by noted photographer and author Steven Foster, and subscriptions to and back issues of *HerbalGram*.

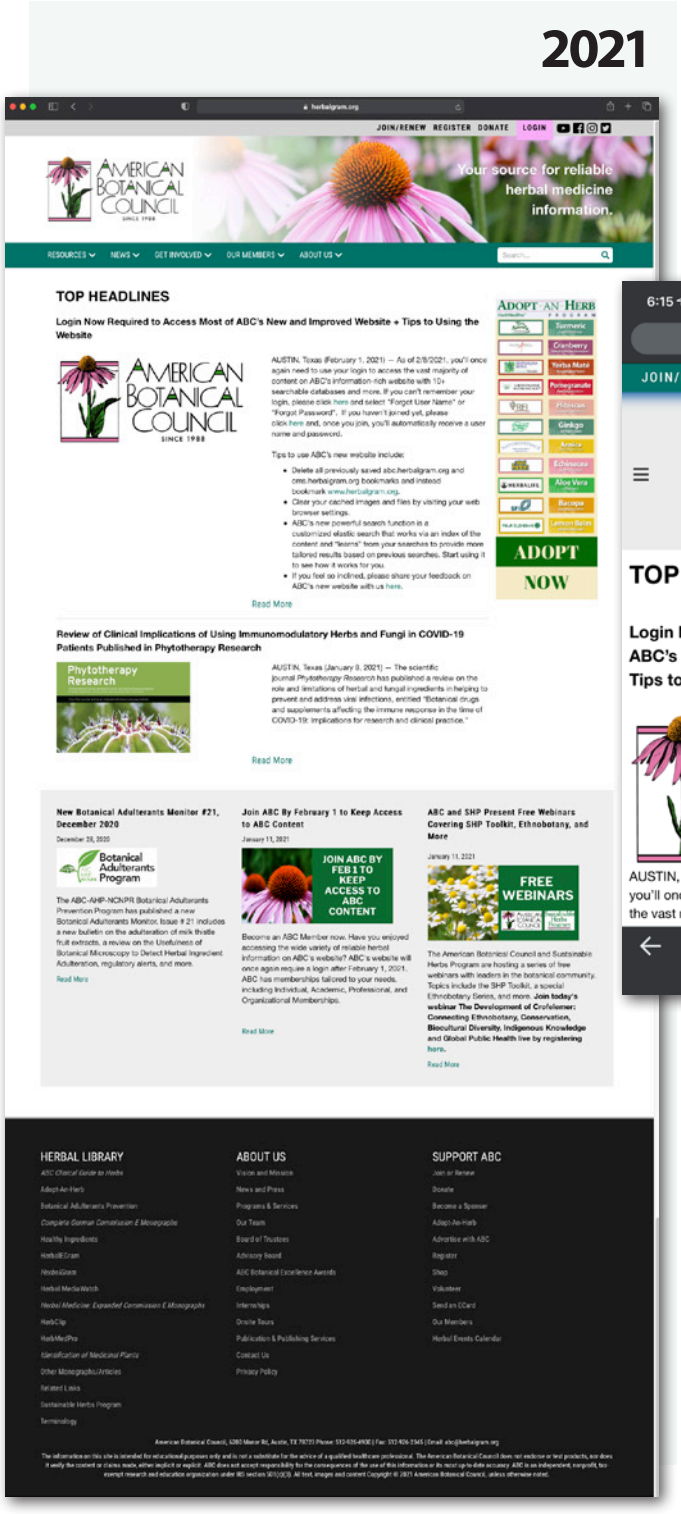
In addition to offering online ordering, the site had grown to include sample content from *HerbalGram*, HerbClip (scientific and clinical article summaries and reviews), ABC's first two books — *The Complete German Commission E Monographs* and *Herbal Medicine: Expanded Commission E Monographs* — and the Botanical Booklet series. The site also included the first iteration of ABC's "Educational Links" pages with hundreds of links to other sites that covered topics such as consumer information, family health, professional organizations, and more.

However, ABC was not yet able to put full content from *HerbalGram*, HerbClip, and its other publications online. While content management systems (CMSs) were available as early as 1995, open-source CMSs and content management frameworks (CMFs) were not widely available until the early 2000s. Realizing the increasing importance of its online presence, ABC contracted with Interactive Ensemble (IE), an Austin, Texas-based web design and development company, to create a new website using a CMS designed by IE that allowed staff to monitor and update dynamic content (i.e., content that

2012



is added regularly). The new site launched in summer 2001 and had an enhanced design that allowed for easier viewing and speedier navigation. As ABC had become a membership-based organization in January 2001, the website also featured a login option that allowed members to access password-protected materials based on their membership level.



In August 2001, ABC's new website earned another honor for its content and design. It was one of six "Complementary and Alternative Therapies" websites recommended in *The Nurses' Guide to Consumer Health Websites* (Springer Publishing Company, 2001). The guide featured 40 categories of consumer-friendly websites with high-quality content that were chosen by nurses with relevant expertise.[2]

In autumn 2006, ABC contracted with Convio (now called Blackbaud, Inc.), a leading software company specializing in internet marketing solutions for nonprofit organizations. Convio's Luminate Online software provided improved security for online membership and book sales, improved e-commerce tools, a constituent management option, and a platform for email campaigns, newsletters, and other outreach efforts.

ABC also needed a new, advanced CMS because of the ongoing increase in ABC's dynamic content and the addition of HerbMedPro, a comprehensive, interactive online database that provides access to important scientific and clinical research data on the uses and health effects of more than 265 herbs, spices, medicinal plants, and fungi. In late 2007, ABC's IT consultant Eric Valdez (Corsair USA, LLC; Austin, Texas) contracted with a web developer (KYUBE/Simplify) to design a new CMS and website to ABC's specifications. The updated website launched in July 2008, taking ABC's content, site navigation, and other online capabilities to the next level. The CMS served ABC well for 10 years until, after a series of technical issues that affected the website's functionality, ABC management and the Board of Trustees prioritized the creation of a new, mobile-responsive site.

Now

In June 2018, Valdez again contracted with a web developer (Capella Solutions; Houston, Texas) to help ABC address site functionality, adapt an open-source CMS called Umbraco to ABC's needs, design a site that would be responsive across mobile devices, and clean up and migrate the website's vast content. Due to the site functionality issues, the large amount of content on the site, and ABC's commitment to accuracy and excellence, it took longer than expected to design, test, and

The new website layout is designed to be more visually appealing and easier to read, due to its cleaner format. It also allows for more graphics to accompany the text. ABC staff expects to add more of Foster's compelling medicinal plant photographs over the coming months

implement the new CMS and website. ABC management decided to launch the new site in January 2021, despite some remaining tasks.

Features of the new ABC website

While the design team continues to improve the responsiveness of the site, users can now view ABC's website on most mobile devices, and the site automatically adapts to the size of the screen. The navigation of the site is intuitive regardless of the device being used.

ABC content is now found in a drop-down navigation menu at the top of the page and in a mega-menu that appears at the bottom of pages. While the previous website was considered state of the art when it was launched in 2008 (the year after Apple introduced the iPhone), the layout became less practical over the years. The new design and supporting CMS address this issue, and previously hard-to-find items are now prominently displayed.

The ABC website has more than 62,500 distinct pages in 11 resource sections, most of which are updated on a regular basis. ABC's HerbMedPro database alone, which is updated weekly, contains more than 132,000 entries. A website of this size and complexity needs a powerful search engine with full-text search capability. The search function on ABC's new site is a customized (and customizable), elastic search that works via an index of the content and "learns" from users' searches to provide tailored results based on previous searches. It can autocomplete searches, if users allow it, or provide a search suggestion, which can be helpful when users are unfamiliar with the spelling of an author or herb name, for example. The search results default to the most relevant results (those that include the search terms the most) but can be filtered by resources (*HerbalGram*, HerbClip, etc.), and chronologically, with the newest results at the top of the list.

The new website layout is designed to be more visually appealing and easier to read, due to its cleaner format. It also allows for more graphics to accompany the text. ABC staff expects to add more of Foster's compelling medicinal plant photographs over the coming months.

ABC's new CMS is state of the art and enables application programming interface (API) software to seamlessly connect with customer relationship management (CRM), bulk email, and e-commerce tools. The site now has the infrastructure to deploy specialized mobile applications and globally syndicated searchable content to numerous licensees and university and other libraries. Finally, the new CMS is much more intuitive and user friendly. This will make adding content to ABC's website much easier for staff and contractors.

The Future

The web design team expects to finish outstanding tasks on the new site by spring 2021. After that, they will begin work on the next phase of ABC's web development project, which includes:

- As part of the 10th anniversary of the Botanical Adulterants Prevention Program (BAPP), the BAPP section of ABC's site will be updated to include new content sections. Functionality will be added later to help users more easily find content within these sections, including upcoming publications.
- Reflecting ABC's stewardship of the Sustainable Herbs Program (SHP), the SHP site will be moved to the new Umbraco platform to make it easier to maintain and add new educational content.
- To improve functionality of the national HerbDay website, which ABC has been managing since 2008, www.HerbDay.org will also be moved to the Umbraco platform.

ABC staff hopes that members and other site visitors find the new website to be a pleasant, improved experience. User comments, questions, and suggestions can be submitted at webmaster@herbalgram.org. HG

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ABC Bids Farewell to Ad Man Lance Lawhon After 17 Years

By Hannah Bauman

In December 2020, the American Botanical Council (ABC) mutually parted ways with Lance Lawhon, who had overseen advertising sales for the nonprofit organization's quarterly peer-reviewed journal *HerbalGram* since issue 60 in 2003. For 17 years, Lawhon contacted potential clients to advertise on ABC's website and in *HerbalGram*, sold ad space, and maintained ABC's strict ad review process.

Lawhon was introduced to ABC while working at the management company Rector-Duncan in Austin, Texas. As a member of the sales team, Lawhon attended the first meeting between Rector-Duncan and ABC Founder and Executive Director Mark Blumenthal.

"I have one very distinct memory from that meeting," Lawhon wrote (email, January 15, 2021). "Our proposal kit had '*HerbalGram*' misspelled and I saw Mark reach over and make a correction with his pen. From there, I knew I'd need to keep close watch on my spelling and grammar around him!"

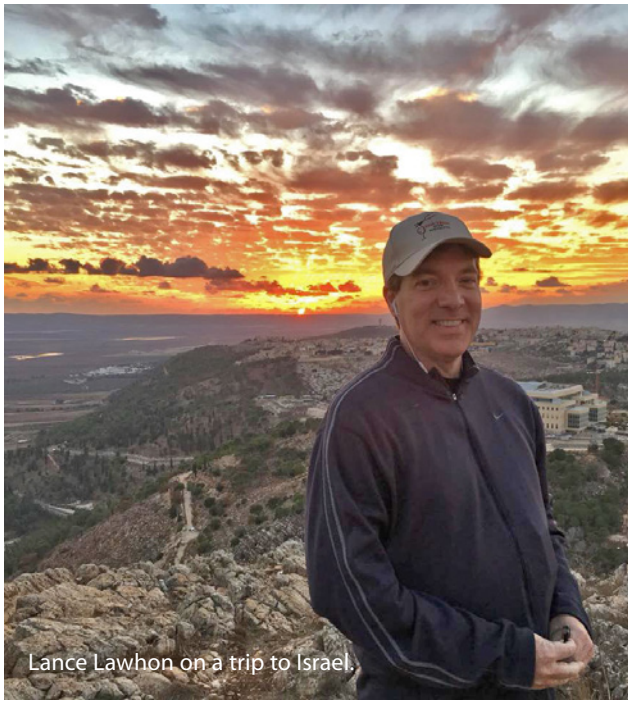
ABC was one of six clients for which Lawhon sold ads, but in 2004, the company downsized, ended its contract with ABC, and laid off Lawhon. Upon contacting ABC to inform them of his change in status, the organization offered him the opportunity to continue working on ad sales in a freelance capacity.

"The thought hadn't even occurred to me. That meant I'd have to start my own business," Lawhon recalled. He did just that, and continued to work with Blumenthal, Art Director Matthew Magruder, and Development Director Denise Meikel.

Initially, Lawhon sold ad space for *HerbalGram* only. But, as the organization's web presence expanded, the scope of his duties grew to encompass advertisements on ABC's website and sponsored email blasts. As part of its commitment to scientific rigor and independently verified information, ABC vets and fact-checks all advertisement claims before publication. During this process, Lawhon served as a liaison between the organization and the advertisers.

"For the entirety of my time with *HerbalGram* and ABC as art director, Lance has been a joy to work with," Magruder commented (email, January 28, 2021). "*HerbalGram* has a unique process of reviewing and approving advertisements in the magazine and Lance has been wonderful in how he navigates this process. He will be missed as a member of our little team. As a fellow artist, I feel compelled to point out that Lance is also an incredibly talented artist. I proudly own one of his sketches from Europe that he gifted me many years ago."

Lawhon, one of the self-proclaimed "five remaining native Austinites" in Austin, is a multi-talented individual with a thriving promotional products business focused on Texas wineries, Spectrum Wine Specialties, which he runs with his parents. When he is not working, he enjoys studying theology, listening to podcasts, cooking, gardening, writing, and playing table-top role-playing games. The growth of his promotional business prompted his retirement from ABC and *HerbalGram*, as he felt he did not have the time necessary to devote to ABC's advertising needs.



Lance Lawhon on a trip to Israel.

Lawhon says he will miss strolling around the 2.5 acres of gardens at the organization's headquarters at the Case Mill Homestead in East Austin. However, he will miss the people most of all, and appreciated being treated like "part of the family" whenever he visited. ABC's passion for its mission, he wrote, was "infectious" and gave him a new perspective on herbs and their uses.

"Working with ABC stretched me as a sales manager and communicator," Lawhon concluded. "I grew up a lot in those 17 years! But to sum up my feelings I can think of only one word: gratitude. I am thankful to have worked with such a passionate and caring group of people. I will always look on my time with ABC with thanks. Whenever I go out into my garden to pick thyme, oregano, or snap off a piece of ginger root, I'll think of my friends at the American Botanical Council."

ABC wishes Lance much success in his future business endeavors. He has already agreed to maintain a relationship with ABC by contributing his popular chocolate cayenne cookies at ABC's annual winter holiday cookie exchange. HG

The Top 10 HerbalEGram Articles of 2020

By ABC Staff

Each January, the editorial staff of the American Botanical Council (ABC) compiles a list of the 10 most popular HerbalEGram articles from the previous year, as determined by the number of individual link clicks. The list reflects the topics that interested the organization's diverse audience of researchers, educators, health care professionals, industry members, the media, and other members of the public.

The top 10 HerbalEGram articles of 2020 included two stories on the impacts of the COVID-19 pandemic on the supply chains for botanical ingredients; reports about global issues including the kava (*Piper methysticum*, Piperaceae) trade in Vanuatu and the alleged racial motivation behind the murder of a Maya healer; a review of a documentary that extols the potential benefits of fungi; and several installments from ABC's ongoing Food as Medicine series, a project helmed by ABC Education Coordinator Jenny Perez in collaboration with *HerbalGram* Associate Editor Hannah Bauman that presents research on health-promoting foods that consumers commonly find in local grocery stores.

The most-clicked HerbalEGram article of 2020 was a Food as Medicine article about black elder berry (*Sambucus nigra*, Adoxaceae). All parts of the elder plant, including its flowers and root bark, have been used for medicinal purposes, but many people associate the dark-purple fruits with cold and flu season because of their immune-regulating properties. The article was published in February at the height of the cold and flu season in the United States and as the COVID-19 virus was spreading rapidly around the world. Author Perez took a deep look into the folk traditions of elder berry and the progress modern research is making to determine its mechanisms of action.

The second-most-clicked story, by HerbalEGram guest contributor Karen Raterman, investigated the impacts of COVID-19 on the supply chain for herbal supplement ingredients. Raterman interviewed many representatives from botanical suppliers and supplement manufacturers about this ongoing situation and learned how these companies are balancing the safety of their workers, the unprecedented surge in demand seen in March and April 2020, the challenge of sourcing ingredients, and how, moving forward, these challenges may help build a stronger industry.

Below is the full list of HerbalEGram's 10 most popular stories of 2020. All articles can be found on ABC's website at https://herbalgram.org/resources/herbalegram/.

1 Food as Medicine: Black Elder Berry (*Sambucus nigra*, Adoxaceae)

By Jenny Perez (February 2020)

Once called the "medicine chest of the country people," the elder shrub has long been a source of food and medicine and is associated with longevity and vitality. Every flu season, many people turn to preparations made from its deep-purple berries to ward off and shorten the duration of flu symptoms. With a tradition of medicinal use that spans centuries, elder berries are becoming one of the most popular immune system strengtheners in the world.

2 Herbal Companies Brace for Supply Chain Impacts of COVID-19

By Karen Raterman (April 2020)

The economic impacts of the COVID-19 pandemic have yet to be fully realized, but many business sectors, including the herbal industry, have already experienced significant disruptions. As the virus continues to spread around the world, many consumers have turned to herbal products marketed or traditionally used for immune health benefits. This surge in demand, particularly for herbal materials usually sourced from China, the original epicenter of the outbreak, has forced many companies to look for new suppliers or alternative formulas. Despite these unprecedented challenges, responsible members of the herbal industry remain optimistic and committed to delivering quality products for consumers.

3 Food as Medicine: Cashew (*Anacardium occidentale*, Anacardiaceae)

By Jenny Perez (October 2020)

The curious case of the cashew: It belongs to the same family as poison ivy (*Toxicodendron* spp.), grows at the end of a pseudofruit, and goes through a lengthy processing procedure to reach store shelves. Cashew is high in fat and also contains fatty acids, tannins, and other polyphenols that may aid a number of metabolic conditions with minimal impacts on weight gain.

4 The Rising and Falling Fortunes of Vanuatu Kava

By Chris Kilham (July 2020)

"Medicine Hunter" Chris Kilham traveled to the Republic of Vanuatu, an island country in the South Pacific, in February 2020 to gain a better understanding of the kava trade there. Kava root, which has prized anxiolytic and sedative properties, is the source of a traditional beverage that has been an important part of South Pacific culture for thousands of years and, more recently, has gained international attention. Kilham has monitored the kava trade in Vanuatu since 1995, but Cyclone Harold in April 2020 and the COVID-19 outbreak have created a unique situation and hardships for kava farmers, producers, and exporters.

5 US Supplement Sales Rise Sharply during First Six Months of 2020

By Tyler Smith (August 2020)

In the first half of 2020, some ingredients traditionally used for immune support saw dramatic sales increases, by percentage, compared to the same time period in 2019, which suggests that many consumers may have turned to natural remedies to help maintain and protect their health, especially at the beginning of the COVID-19 pandemic, despite the limited published research on botanicals for COVID-19.

6 Food as Medicine: Hibiscus (*Hibiscus sabdariffa*, Malvaceae)

By Jenny Perez (August 2020)

Bright red and pleasingly tart, the hibiscus flower has become popular in tropical climates as part of a cooling beverage in warm weather and a seasonal cranberry (*Vaccinium macrocarpon*, Ericaceae) replacement in the winter. Traditionally, hibiscus was used for its anti-inflammatory, diuretic, and fever-lowering actions. Based on these traditional uses, modern research is studying hibiscus as a potential cardioprotective aid, metabolic aid, and more.

7 The Murder of Maya Healer Domingo Choc Che: A Q&A with Mónica Berger Gonzalez and Michael Heinrich

By Connor Yearsley (September 2020)

In early June 2020, Domingo Choc Che, a Maya traditional medicine expert, allegedly was accused of witchcraft and burned alive by a group of people in Chimay, Guatemala. At the time of his death, he was part of a project to document traditional medicinal plants in the Petén department of Guatemala. Choc Che's murder reflects longstanding racism and ignorance in the region and reinforces the importance of projects like the one he was working on. This article includes a Q&A with two of Choc Che's colleagues, who provide insights about who he was and what should be learned from his murder.

8 Less Gas with Lemongrass? Burger King Aims to Reduce Methane with Modified Cattle Diet

By Connor Yearsley (October 2020)

In July 2020, the "reduced-methane" Whopper® debuted at select Burger King locations in the United States. The burger is sourced from cattle that were fed lemongrass (*Cymbopogon citratus*, Poaceae), which Burger King claims has the potential to reduce methane emissions from those animals by up to 33%. The initiative has created some controversy, but it may be a step in the right direction for reducing emissions that contribute to climate change.

9 *Fantastic Fungi* Film Explores the Magic and Mystery Underneath Your Feet

By Connor Yearsley (April 2020)

Fungal species greatly outnumber plant species and have existed longer than land plants, but people often forget about fungi, which help ecosystems flourish. *Fantastic Fungi: The Magic Beneath Us*, a documentary that features notable naturalists like Paul Stamets, explores the complexity, diversity, and versatility of fungi. The film shows that fungi and their derivatives can alleviate existential distress, break down oil, filter water, and much more.

10 Food as Medicine: Moringa (*Moringa oleifera*, Moringaceae)

By Jenny Perez (April 2020)

All parts of the moringa plant, including its long, alien-looking pods, have been used medicinally in Asia, including India, and Africa, but moringa leaf specifically may provide a solution to malnutrition and maternal health in underserved communities. Drought resistant and packed with vitamins, minerals, and protein, moringa has been labeled as a plant that "might save the world." HG

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For more details on joining the program, and access to the free publications produced to date, **please see www.botanicaladulterants.org or contact Denise Meikel at denise@herbalgram.org.**

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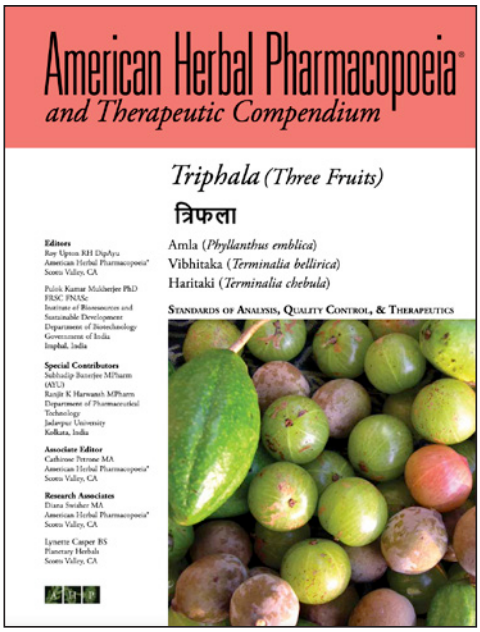
American Herbal Pharmacopoeia Publishes Triphala Monograph and Therapeutic Compendium

By Connor Yearsley

In November 2020, the American Herbal Pharmacopoeia (AHP) released a monograph containing quality control standards and a therapeutic compendium (as one document) for *triphala*, a traditional Ayurvedic herbal formula made from the fruits of amla (*Phyllanthus emblica*, Phyllanthaceae), belleric myrobalan (*vibhitaka*; *Terminalia bellirica*, Combretaceae), and chebulic myrobalan (*haritaki*; *T. chebula*).[1]

Triphala is one of the most important and commonly used formulas in India's traditional medicine system of Ayurveda, which reportedly is the oldest continually used health care system in the world. Triphala, which often is used for gastrointestinal health, is also one of the oldest herbal formulas in continued use and has been used in the same way for more than 2,000 years.

This is the first time AHP has undertaken a monograph and therapeutic compendium for a multi-herb formula. AHP claims that it is the first monograph of its kind in a Western pharmacopeia and the most complete review of triphala's therapeutic and safety profile in English. In January 2019, AHP released an individual monograph and therapeutic compendium for belleric myrobalan fruit, and it is creating individual monographs and therapeutic compendia for amla and chebulic myrobalan fruits, the formula's two other ingredients.



AHP's triphala publication

"Interest in Ayurveda continues to grow, and it seemed appropriate to showcase one of its most important formulas," wrote Roy Upton, RH (AHG), DipAyu, president of AHP and editor of the monograph (email, November 4, 2020). "This monograph is also a natural extension of our work on the individual fruits that make up the triphala formula and are highly regarded in their own right."

AHP monographs establish identification, purity, and quality standards for botanical raw materials and preparations. The therapeutic compendia provide a comprehensive review of pharmacological and safety data, including medical indications and evidence from clinical, animal, and in vitro studies; modern and traditional uses; pharmacokinetics; pharmacodynamics; and guidance for structure and function claims. The compendia also cover dosages, interactions, side effects, contraindications, toxicology, and more. This information can be used by individuals in the herbal community, from consumers and health care practitioners to industry members like quality control personnel, purchasing agents, and dietary supplement manufacturers.

Triphala, which means "three fruits" in Sanskrit, is made of the dried pericarps (coats or hulls) of the fruits in equal parts, unless otherwise specified. Often, whole fruits are traded, but deseeded fruits are preferable. Archaeological evidence suggests that the three fruits were cultivated in northern India as early as 1,000 BCE. The *Caraka Samhita*, which is one of the foundational texts of Ayurvedic medicine and is roughly dated to about the first to second century BCE, mentions triphala, primarily for the intestines and as a rejuvenating tonic (*rasayana*).

The three fruits are said to have five of the six primary flavors recognized in Ayurveda, with the flavor corresponding to pharmacological activity in Ayurvedic tradition. Triphala's primary action is on the gastrointestinal tract, and it has been used as a blood purifier (a common indication in traditional medicine systems), bowel regulator, intestinal cleanser (detoxifier), and eyewash to treat conjunctivitis, redness, and soreness of eyes. It also has been used for constipation, dyspepsia (indigestion), headache, leukorrhea (vaginal discharge), and liver conditions. Paradoxically, it has been used for both diarrhea and constipation.

Modern clinical and pre-clinical evidence indicates that triphala has multiple benefits for gastrointestinal health. For example, it may be able to promote bowel regularity without causing dependence like other laxatives, elicit antioxidant activity in intestinal cells thereby reducing inflammation, heal the brush border of intestinal villi thereby helping leaky gut syndrome, and positively affect the intestinal microbiome, which is important for human health. It may also have antidiabetic and anti-obesity effects and can reduce abdominal pain, flatulence, and hyperacidity.

Belleric myrobalan and chebulic myrobalan also were the subjects of a feature article in *HerbalGram* issue 123.[2] That article describes how a FairWild Standard implementation project in the Western Ghats mountains of India is preserving wild belleric myrobalan and chebulic myrobalan trees and, as a result, the nesting/roosting sites of two rare hornbill

species, which may disperse the trees' seeds. The project was largely made possible by the support of Pukka Herbs in Bristol, United Kingdom, which was also one of the financial and technical supporters of the AHP triphala monograph.

The new triphala monograph was also a collaboration among AHP and researchers at Jadavpur University in Kolkata, India, including Pulok Kumar Mukherjee, PhD, a prominent researcher of Ayurvedic botanicals. In all, 29 co-authors from around the world contributed to the monograph, and 19 experts reviewed it before publication. Work on the monograph began around 2017.

Upton hopes the monograph will make more people aware of the many health benefits associated with triphala, "as no other herbal or medical tradition has anything that matches its uniqueness," he wrote. "Monographing three botanicals in one was a unique challenge, but that was largely overcome by the cadre of experts we brought together to make this a reality. Also, formulas are among the most common preparations used in traditional healing systems. Western pharmacopeias have to begin opening up to the inclusion of classic formulas to adequately recognize the benefits that these systems have to offer.

"There are a variety of grades of individual fruits that make up triphala as well as formulas prepared from fruits in which the pits have been removed (which cost more and are more consistent with traditional practices) and those with pits still intact," Upton added. "Marketers, manufacturers, and practitioners should be aware of the different types that are available so they can make an educated decision regarding sourcing. The pits do not render the formula inactive, but they may render it less active for some people because the pits add a lot of weight to the fruit (approximately 50%), and the constituent profile in the pits is much less than in the fruits themselves."

Sebastian Pole, cofounder of Pukka Herbs, wrote: "Ayurveda's contribution to how we understand and manage health is exemplary, but Ayurveda faces challenges, as all herbal traditions do, in relation to sustainability and consistent quality standards across the value chain. AHP's best-in-class monograph shines a light on the fundamental value that traditional medical knowledge can bring to so many of today's urgent health care needs. It is vital for everyone involved in the herbal tradition that the quality, safety, and therapeutics of nature's pharmacopeia are thoroughly assessed. This is also true with triphala, one of the most popular herbal formulas, whose history, character, and uniqueness are described so expertly in AHP's monograph" (email, November 10, 2020).

"The reputation and effectiveness of herbal medicine depend on the plants' being as exemplary as the traditions of which they are part," Pole added. "Just because triphala is popular does not mean that every batch is high quality or sustainably harvested. This monograph will help ensure that high standards are met. Three cheers for the three fruits and AHP."

The triphala monograph is the 42nd monograph published by AHP since 1998. It is available for purchase through AHP's website[1] and was made possible by the financial support of Aveda Corporation, Banyan Botanicals, East West School of Planetary Herbology, EuroPharma USA, Gaia Herbs, Herb Pharm, Nature's Way, NOW Foods, NuAxon Bioscience, Organic India Charitable Trust, Phalada Agro, Planetary Herbals, Pukka Herbs, The Ayurvedic Institute, Traditional Medicinals, Verdure Sciences, and Vikram Naharwar. HG

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The three fruits of Ayurveda's *triphala* formula. Clockwise from top: *Terminalia bellirica*, *Phyllanthus emblica*, and *T. chebula*.
Photo courtesy of Sebastian Pole

Thailand Approves Asian Herb Andrographis to Treat COVID-19

By Connor Yearsley

In late December 2020, the government of Thailand approved a pilot study of the use of the southern Asian herb andrographis (*Andrographis paniculata*, Acanthaceae) to treat early symptoms and reduce the severity of COVID-19. Initially, the treatment will be available at five state-owned hospitals in Thailand on a voluntary basis for people 18-60 years old with minor symptoms. It reportedly will be given to patients within 72 hours of symptom onset. This approval comes amid an increase of COVID-19 infections in the country.[1] As of January 28, 2021, Thailand had 16,221 cases of COVID-19 in a total population of about 70 million.[2]

Called *fah talai jone* in Thai and "the king of bitters," among other names, andrographis is a small annual plant. In India's traditional medical system of Ayurveda, the plant's dried leaves and shoots are used for bronchitis, cough, diarrhea, dyspepsia (indigestion), fever, inflammation, and skin diseases. In traditional Chinese medicine, the plant has been used to treat colitis (inflammatory disease of the colon), cough, dysentery, fever, influenza, and sore throat. Modern studies have focused on andrographis' potential benefits for respiratory and digestive conditions.[3]

In late June 2020, *The Nation Thailand* reported that phase 1 of the Thai research initiative on andrographis for COVID-19 had begun at two hospitals in Thailand. In this preliminary trial, patients received andrographis extract capsules* if they were confirmed to be infected with COVID-19 and had mild to moderate symptoms, including fever and coughing, lasting no more than 72 hours. Six subjects reportedly received 60 mg, or three times the normal dose, of andrographis extract capsules three times per day, while another six subjects received 100 mg, or five times the normal dose, three times per day.[5]

In late August 2020, *The Nation Thailand* reported that the lower dose of andrographis showed benefits in the preliminary trial, especially for coughing. Within three days, both cough volume and overall symptom severity reportedly decreased significantly. After five days, other symptoms improved, and real-time polymerase chain reaction (PCR) tests were negative for the COVID-19 virus in two patients. After three weeks, real-time PCR tests were negative in all six subjects, but additional studies were needed to confirm the results.[6]

Andrographis
Andrographis paniculata
Photo ©2021 Steven Foster

* According to an article published in the *Bangkok Post* in May 2020, "the Department of Thai Traditional and Alternative Medicine signed an MoU [memorandum of understanding] with the Department of Medical Sciences and the Government Pharmaceutical Organisation (GPO) on Feb. 25 for a laboratory experiment. Under the contract, the Institute of Biological Products conducted the test. It used ground dried leaves of andrographis and andrographis extract produced by Thai Herbal Products Company, an affiliate of GPO."[4] However, it is not clear if this is the same andrographis preparation used in the human studies.

Phase 2 was scheduled to begin in September 2020 and reportedly included 60 volunteers who were divided into two groups: one that received andrographis and one that received placebo.[6] Details about the results of this phase are unclear, but in December, when the andrographis extract was approved for the pilot study, the Thai government reportedly claimed that the plant could be used as a safe, effective, less costly treatment alternative for COVID-19 and can reduce inflammation, according to Bloomberg.[1] The plants used in the Thai COVID-19 research initiative are being sourced from Thailand.[5]

In a study published in November 2020, researchers screened 122 Thai natural products (114 medicinal plant extracts and eight purified compounds) for activity against SARS-CoV-2, the virus that causes COVID-19. Among six selected candidates, andrographis extract had moderate inhibitory activity against the virus in cell cultures, while its purified compound andrographolide exhibited 99.9% inhibitory activity against the virus in cell cultures.[7]

Another in vitro study from Thailand published in December 2020 showed that a 95% ethanol extract of andrographis significantly inhibited the production of SARS-CoV-2 in a human lung cell model. The andrographis material met the criteria of the *Thai Herbal Pharmacopoeia*, and its powder was made into an extract using 95% ethanol at a 4:1 ratio.[8] It is unclear if these two studies played a part in the government's approval of andrographis for COVID-19.

In an email notice sent by the American Herbal Pharmacopoeia (AHP) on January 4, 2021, about the Thai government's approval of andrographis, Roy Upton, RH (AHG), DipAyu, president of AHP, was quoted as saying: "Mobilizing immune defenses as soon as symptoms arise is critically important for management of any upper respiratory infection.

"It is a strategy employed by Chinese herbal practitioners for centuries and is a formal part of [COVID-19] treatment protocols in China, where more than 90% of COVID patients are treated with herbs," whereas for many COVID-19 patients in the United States, the disease progresses while waiting for the test results.

According to the AHP notice, COVID-19 "patients in the US [may be] at a distinct disadvantage [by] not integrating herbal medicines into the management of COVID-19." HG

Other Potential Benefits of Andrographis

Previous studies have found that andrographis may have benefits for other viral infections. A 2004 study that involved 133 children with the common cold compared a preparation of echinacea (*Echinacea purpurea*, Asteraceae) in combination with standard conventional medical treatment, a preparation containing andrographis in combination with standard treatment, and standard treatment only. All three groups experienced improvements in upper respiratory symptoms, but the children who received the preparation containing andrographis recovered from symptoms significantly faster than children in the two other groups.[9]

A 2017 systematic review that included 33 randomized, controlled trials (N = 7,175) suggested that andrographis may have benefits for acute respiratory tract infections (ARTIs). Andrographis improved cough and sore throat compared to placebo and significantly improved overall symptoms of ARTIs compared to placebo and other herbal treatments. The meta-analysis of 12 clinical studies comparing andrographis to usual care (conventional treatment with analgesics, antibiotics, anti-inflammatories, antivirals, corticosteroids, or steroids) indicated a statistically significant reduction in the duration of sore throat and sick leave, but not cough. No major adverse events (AEs) were reported, while minor AEs were mostly gastrointestinal. However, the overall methodological quality of included studies was rated "poor."[10]

Andrographis is the main ingredient of the multi-herb formula *Nilavembu Kudineer*, which is used in Siddha medicine of India and also includes nutgrass (*Cyperus rotundus*, Cyperaceae), threadstem carpetweed (*Mollugo cerviana*, Molluginaceae), black pepper (*Piper nigrum*, Piperaceae), Indian sandalwood (*Santalum album*, Santalaceae), snake gourd (*Trichosanthes cucumerina*, Cucurbitaceae), vetiver (*Vetiveria zizanioides*, Poaceae), and ginger (*Zingiber officinale*, Zingiberaceae). Traditionally, these plants have been used to treat arthralgia (joint pain), arthritis, fever, gastric ulcers, general debility, inflammation, and jaundice. In a 2018 study, an ethanolic extract of Nilavembu Kudineer provided protection against dengue virus (a flavivirus) and chikungunya virus (an alphavirus) during active infection and helped prevent viral infection in cell cultures that were pre-treated with the formula.[11]

In a 2018 study, arthritic rats were given andrographolide combined with the conventional drug methotrexate, which can be hepatotoxic. Another group of rats received methotrexate only and another group received andrographolide only. Andrographolide improved the anti-arthritic effect of methotrexate. The combined therapy additively reduced inflammatory symptoms in the rats and significantly alleviated hepatocellular injury induced by methotrexate, according to the authors.[12]

In a 2019 study, pre-treatment with andrographolide sulfonate (AS), a water-soluble form of andrographolide, significantly attenuated lung injury and infiltration of inflammatory cells in mice infected with the bacterium *Klebsiella pneumoniae*, which is a major cause of respiratory infections. Mice treated with AS alone died after six days of infection, while a control group that received only the antibiotic imipenem had a survival rate of 33.3% after 15 days of infection. However, AS combined with imipenem resulted in 100% survival after 15 days of infection. This suggests that AS could synergistically improve the efficacy of imipenem.[13]

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Review Finds CBD Has Therapeutic Potential for Anxiety Disorders

Reviewed: Skelley JW, Deas CM, Curren Z, Ennis J. Use of cannabidiol in anxiety and anxiety-related disorders. *J Am Pharm Assoc*. January-February 2020;60(1):253-261. doi: 10.1016/j.japh.2019.11.008.

By Mariann Garner-Wizard

Study Details: At a Glance	
Study Design	Systematic review
Included Studies	Six randomized, placebo-controlled clinical trials, one case report, and one case series
Test Materials	CBD capsules in a range of dosages (25 mg/day to 900 mg/day)
Controls	Various
Disclosures	The authors declared no conflicts of interest.

Anxiety, generally defined as a natural response to perceived threats, becomes maladaptive in excess or in the absence of threats. Neuroimaging and biochemical studies suggest that the balance between adaptive and maladaptive anxiety is modulated by regions of the brain called the limbic system, mainly the amygdala, and key neurotransmitters that act on nerve cells in the amygdala and other areas. Anxiety disorders (ADs) include social AD (SAD), generalized AD (GAD), panic disorder, specific phobias, and separation anxiety. Obsessive-compulsive disorder (OCD) and post-traumatic stress disorder (PTSD), which can have similar symptomology, are diagnosed separately. Together, ADs and anxiety-related disorders are the most common psychiatric disorders in the United States. They are associated with decreased well-being, severe emotional distress, physical impairment, loss of productivity, and higher health care costs.

The main pharmacological treatments for anxiety and ADs modulate activity of various neurotransmitters. Less-common treatments include second-generation antipsychotics, anticonvulsants, and some antihistamines. All have limited efficacy and may cause adverse effects (AEs).

The endocannabinoid system (ECS), a biochemical signaling system, is a target for anxiolytic drugs due to its role in modulating nerve-to-nerve communication and synaptic plasticity (changes in the activity of synapses, the gaps between neurons through which electrical and chemical signals pass) in the anxiety response. The ECS includes two known cannabinoid (CB) receptors: CB1 and CB2. Cannabidiol (CBD), a psychoactive but nonintoxicating phytocannabinoid from cannabis (*Cannabis sativa*, Cannabaceae), has low affinity for both CB receptors. CBD is believed to indirectly affect the ECS by suppressing the inactivation of anandamide, an endogenous (internally originating) ECS neuromodulator, which in turn activates CB1 receptors. CBD also affects serotonin (5-HT) receptors.

Few studies have examined CBD's potential for AEs and drug interactions versus other agents, but available evidence suggests that CBD has a favorable safety profile. CBD can be administered orally or topically and is available in tinctures, oils, topical creams, vaporization agents, and infused foods and beverages. Only one CBD product, Epidiolex® (GW Pharmaceuticals; Cambridge, England), a standardized oil-based CBD oral solution, is approved as a drug by the US Food and Drug Administration (FDA). Other cannabis-derived CBD products are regulated by the FDA under the 2018 Farm Bill, and, as the review authors noted, "determination of the scope of this regulation is evolving."

The authors conducted a systematic review of evidence for CBD's safety and efficacy in anxiety and ADs, following the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines. An electronic database search of PubMed, Google Scholar, and International Pharmaceutical Abstracts for studies between January 1996 and June 2019 found 233 potentially relevant reports. Nine were added from references. Studies were included if they reported CBD treatment of anxiety or ADs or assessed the effects of CBD on anxiety response in healthy humans. In vivo assays and clinical studies that evaluated psychosis-related components of PTSD or OCD, or the role of CBD in modulating cannabis-related intoxication, were excluded. After screening the articles, eight met all the inclusion criteria. They included six randomized, placebo-controlled clinical trials (RCTs), a case report, and a case series (a type of observational study).

In a double-blind, crossover RCT, 10 healthy men who took a single dose of 400 mg CBD had significant reductions in anxiety ($P < 0.001$) assessed by visual analog scale (VAS) at all time points (30, 60, and 75 minutes after ingestion). The subjects also had significantly increased regional cerebral blood flow (rCBF) in the medial temporal cortex ($P < 0.001$), as assessed by single-photon emission computed tomography, a neuroimaging technique. Sedation was mentioned as an AE, but the frequency and severity of this AE were not reported.

In another double-blind RCT, 59 healthy men and women with no diagnosed AD or alcohol- or drug-related disorders were randomly assigned to one of five groups: 100 mg CBD, 300 mg CBD, 900 mg CBD, 1 mg clonazepam (a benzodiazepine), or placebo. VAS scores measuring subjective anxiety and sedation and vital signs were recorded at baseline and before, during, and after a simulated public speaking (SPS) exercise. After the speech, VAS scores were significantly lower in the 300 mg CBD group compared to the placebo and 100 mg CBD groups ($P < 0.05$ for both). Anxiety during the speech decreased significantly more from baseline in the 300 mg CBD group versus the 900 mg group ($P < 0.05$). Clonazepam was significantly more sedating than the different doses of CBD ($P < 0.05$ for all) during all phases of the SPS.

The authors noted that the results were in line with previous findings and suggested "that CBD induces acute anxiolytic effects with an inverted U-shaped dose-response curve in humans — an effect that, at this time, is not fully understood." In other words, increasing doses of CBD correspond to increased effects until a maximum point is reached, after which effects begin to decrease as the CBD dose continues to increase. Another double-blind RCT using VAS scores and an SPS exercise supported this inverted U-shaped dose response, with 300 mg CBD having more of an anxiolytic effect than 150 mg or 600 mg CBD in 57 healthy men.

In another double-blind RCT, 40 healthy adults were separated into four groups of 10 that received 300 mg CBD, 10 mg diazepam (a benzodiazepine), 5 mg ipsapirone (an antidepressant and anxiolytic), or placebo before an SPS exercise. VAS scores indicated that CBD significantly reduced post-SPS anxiety versus placebo (P = 0.017). Ipsapirone significantly reduced performance anxiety versus placebo (P = 0.037). Diazepam significantly reduced anxiety throughout the study when compared to placebo (P = 0.016 overall), but the authors noted that the associated physical and mental sedation limited its usefulness despite its efficacy.

A double-blind RCT evaluated 600 mg CBD versus placebo in 24 patients with SAD and compared the effects with 12 healthy controls who received no study agent. Subjective and physiological measures were used in an SPS exercise. Patients with SAD who received placebo had significantly higher anxiety than healthy controls (P value not stated). The CBD group had significantly less anxiety during the SPS exercise compared to the placebo group (P = 0.009).

An open-label case series of 72 adults with anxiety or sleep disorders in an outpatient psychiatric clinic observed the effects of prescribed daily doses of CBD (ranging from 25 mg to 175 mg) for up to three months. Anxiety was assessed at baseline and monthly follow-ups via the Hamilton Anxiety Rating Scale (HAM-A). Patients were included if they had at least one follow-up visit after CBD was prescribed. At one month, 79.2% of patients' HAM-A scores had improved over baseline. At two months, 78.1% of those assessed had improved compared to the previous month. Third month scores did not differ significantly from second month scores. AEs included sedation, dry eyes, fatigue, and increased sexually inappropriate behavior. A few subjects with fatigue and sexual inappropriateness stopped CBD. The study concluded that CBD reduced anxiety over the period used, had a sustained effect, and was well-tolerated.

The included case report described the effects of CBD on PTSD-related anxiety in a 10-year-old girl, who did not respond to previously prescribed pharmacotherapy. The patient received 25-mg capsules of CBD oil daily for four months, after which she also received a sublingual spray to take for anxiety as needed (6-12 mg CBD per spray). Anxiety was assessed using a self-report scale at baseline and once per month for five months. From baseline to the last assessment, anxiety scores decreased by 47%. No AEs were reported.

In the eight studies reviewed, CBD regularly produced improvements in SAD, GAD, and anxiety related to PTSD. However, the small sample sizes, low statistical power of many of the studies, and use of subjective self-report measures, among other limitations, make it necessary to interpret results with caution. These authors also did not provide a quality assessment of included studies. HG

CBD oil and *Cannabis sativa*
Photo ©2021 Matthew Magruder

Elder Berry Extract May Reduce Symptoms of Acute Respiratory Viral Infections

Reviewed: Harnett J, Oakes K, Caré J, et al. The effects of *Sambucus nigra* berry on acute respiratory viral infections: A rapid review of clinical studies. *Adv Integr Med*. December 2020;7(4):240-246. doi: 10.1016/j.aimed.2020.08.001.

By Samaara Robbins

European elder (*Sambucus nigra*, Adoxaceae) berries and flowers have been used traditionally to treat common colds and the flu. Elder berry extracts have been shown to have antimicrobial and antiviral properties. Some preclinical studies have shown that elder berry extracts demonstrate positive effects against influenza virus infection, specifically by inhibiting viral replication and increasing both pro-inflammatory and anti-inflammatory cytokines involved in the immune response. The purpose of this review was to determine whether elder berry extract improves outcomes in patients with acute respiratory viral infections (ARVIs).

A keyword search was performed for articles in MEDLINE, Embase, the Allied and Complementary Medicine Database, and the Cumulative Index to Nursing and Allied Health Literature database from inception through May 2020. Included articles were original prospective intervention studies using adult participants with ARVIs, written in English, and evaluated elder berry (as a mono- or combination therapy) in any form, dose, and route of administration. Studies that involved children only or participants with fungal or non-infectious respiratory diseases were excluded. Forty studies initially were identified and five met all inclusion criteria.

The pooled sample size was 936 participants between five and 70 years of age, with two studies also including both children (5-12 years of age) and adults (18 years of age and older). The included studies were conducted in Australia (n = 1), China (n = 1), the Czech Republic (n = 1), Israel (n = 1), and Norway (n = 1). The conditions studied included influenza (n = 2), influenza-like symptoms (n = 2), and the common cold (n = 2).

Four studies used mono-herbal preparations of elder berry extract, and one study used a poly-herbal blend of elder berry and echinacea (*Echinacea purpurea*, Asteraceae) root (Table 1).

Study Details: At a Glance	
Study Design	Review
Included Studies	Five randomized, controlled clinical trials (N = 936)
Test Materials	Mono-herbal preparations of elder berry extract (four studies) or a poly-herbal blend of echinacea root and elder berry (one study)
Controls	Various
Disclosures	The authors declared no conflict of interest.

Two of the five studies showed "some concern" for bias according to the Cochrane risk of bias assessment tool; the remaining three studies reported a low risk of bias. A meta-analysis was not conducted due to heterogeneity of the data.

In general, significant reductions of symptoms and shorter duration of illness were observed in the mono- and poly-herbal groups compared to the control groups. All studies reported a significant reduction in the severity of overall symptoms and fever specifically, and one study also reported significant reductions in cough, headache, mucus discharge, muscle ache, and nasal congestion symptoms.

Duration of illness was reported in four studies, with consistent outcomes. The poly-herbal study reported a similar, non-inferior rate of recovery compared to oseltamivir (an antiviral medication). Three studies reported an almost 50% reduction in duration of illness in the elder berry groups versus the control groups. Two studies reported the use of rescue medications (including analgesics, antibiotics, cold tablets, and nasal sprays) in elder berry and control groups, but the need for these medications was not consistent.

Table 1. Elder Berry Preparations Used in Reviewed Studies

Preparation	Used in	Manufacturer	Dosage
Sambucol® syrup containing 38% elder berry extract	Two studies	Razei Bar Industries (Jerusalem, Israel)	15 mL syrup up to four times per day
Capsules containing 300 mg BerryPharma® elder berry extract	One study	Iprona AG (Lana, Italy)	Three capsules per day
Lozenges containing 175 mg of a proprietary elder berry extract	One study	HerbalScience Singapore Pte. Ltd. (Singapore)	175 mg lozenge four times a day
Echinaforce® Hot Drink containing 240 mg echinacea root and 276.5 mg elder berry	One study	A. Vogel AG (Roggwil, Switzerland)	5 mL five times a day for three days followed by maintenance dose twice a day for seven days

No serious adverse events were reported. Adverse events included cold-like symptoms, fatigue, itchy throat, and kidney pain. Nausea and vomiting were reported in the study using the poly-herbal blend.

The authors conclude that mono-herbal preparations of elder berry extract, when taken at the onset of symptoms and for up to two weeks, may provide relief from symptoms of the common cold and influenza. They also note that elder berry extract may be effective in reducing duration and severity of fever, headache, nasal congestion, and nasal mucus discharge associated with ARVIs. However, the "evidence regarding the effectiveness of *S. nigra* berry on the symptom of cough, and need for/use of medicines (including antibiotics) to treat ARVIs, is currently unclear and inconsistent," they explained.

As the formulation, dose, and duration of elder berry treatment varied across studies, additional research is needed to further evaluate the efficacy and safety of elder berry extracts for ARVIs. HG

Elder berry *Sambucus nigra*. Photo ©2021 Steven Foster

Korean Ginseng May Improve Fatigue and Cognitive Function of Adults Who Perform Full-Time Computer Work

Reviewed: Mariage PA, Hovhannisyan A, Panossian AG. Efficacy of *Panax ginseng* Meyer herbal preparation HRG80 in preventing and mitigating stress-induced failure of cognitive functions in healthy subjects: A pilot, randomized, double-blind, placebo-controlled crossover trial. *Pharmaceuticals*. March 29, 2020;13(4):57. doi: 10.3390/ph13040057.

By Heather S. Oliff, PhD

The purpose of this three-arm, randomized, double-blind, placebo-controlled crossover study was to assess the safety and efficacy of two standardized Asian ginseng (*Panax ginseng*, Araliaceae) preparations in reducing symptoms of occupational stress such as fatigue, impaired memory, difficulty with concentration, and attention deficit in healthy adults.

The authors recruited healthy men and women (N = 50, aged 18-65 years) who performed full-time work as teleoperators or in information technology with work-related stress and fatigue. All participants had occupational stress beyond normal limits according to the Perceived Stress Scale (PSS), but none were categorized as having pathological stress. Exclusion criteria included use of over-the-counter medications or dietary supplements that may impact cognitive function, consumption of more than one cup of coffee (*Coffea* spp., Rubiaceae) daily, allergy to ginseng (*Panax* spp.) preparations, or "any other condition that precluded participation according to the judgement of the investigator."

The two ginseng preparations used were red* Asian ginseng (RG) root powder (HRG80™; Botalys SA; Ath, Belgium) capsules and white Asian ginseng (WG) root powder capsules (Arkopharma

Study Details: At a Glance	
Study Design	Three-arm, randomized, double-blind, placebo-controlled crossover study
Participants	Healthy adults (N = 50) with symptoms of stress and fatigue
Test Materials	*Panax ginseng* root powder (HRG80™; Botalys SA; Ath, Belgium) capsules and *Panax ginseng* root powder capsules (Arkopharma Laboratories; Carros, France)
Controls	Placebo capsules containing brown sugar and rice flour
Disclosures	PAM is the co-CEO of Botalys SA and AGP is an independent contractor for Europharma USA (a study funder) and head of research and development for Phytomed AB.

* "Red" Asian ginseng roots are typically steamed, which turns the roots a reddish-brown color, before drying. "White" Asian ginseng refers to roots that have been washed and then dried in the sun or an oven.

Asian ginseng *Panax ginseng*. Photo ©2021 Steven Foster

Laboratories; Carros, France). The 418-mg RG capsules contained 209 mg powdered Asian ginseng root and 209 mg of inactive excipient rice (*Oryza sativa*, Poaceae) flour and were standardized to contain 31.7 mg ginsenosides (including 25.9 mg "rare ginsenosides"). The 384-mg WG capsules contained 384 mg Asian ginseng root powder with 9.9 mg ginsenosides (including 3.056 mg "rare ginsenosides").

Participants were randomly assigned to one of three groups: RG (n = 17), WG (n = 16), or placebo (n = 17) capsules, which contained 418 mg of brown sugar (*Saccharum officinarum*, Poaceae) and rice flour. According to the authors, the capsules' appearance, taste, smell, and color were similar and indistinguishable. The participants were instructed to take two capsules once per day with water for two weeks. Compliance was self-reported and measured via pill count.

The primary outcome measure was the error-rate score on the d2 Test of Attention, which is used to assess selective attention, sustained attention, and visual-scanning speed. Secondary outcome measures were the PSS score, which is used to assess perceived stress levels, and the verbal memory accuracy score on the Computerized Memory Flow Level 2 test (MT), which is used to assess cognitive functions (learning, memory, and attention). Assessments were made daily before work and at the end of each eight-hour workday for two weeks. There was a 12-day washout period, and then participants were crossed over to an alternate treatment. All participants received all three treatments each for two weeks with a 12-day washout period between each treatment.

In the placebo group, the error rate on the d2 attention test was significantly increased at the end of a stressful workday. At the end of the workday, the d2 error rate in the RG group was significantly decreased compared with placebo and WG groups ($P < 0.0001$ for both). The d2 error rate in the WG group was not significantly different than the error rate in the placebo group at the end of the workday.

The MT accuracy score significantly decreased from the beginning of the day to end of day in the placebo group ($P < 0.05$), but not the RG and WG groups, and there was no significant difference between ginseng groups.

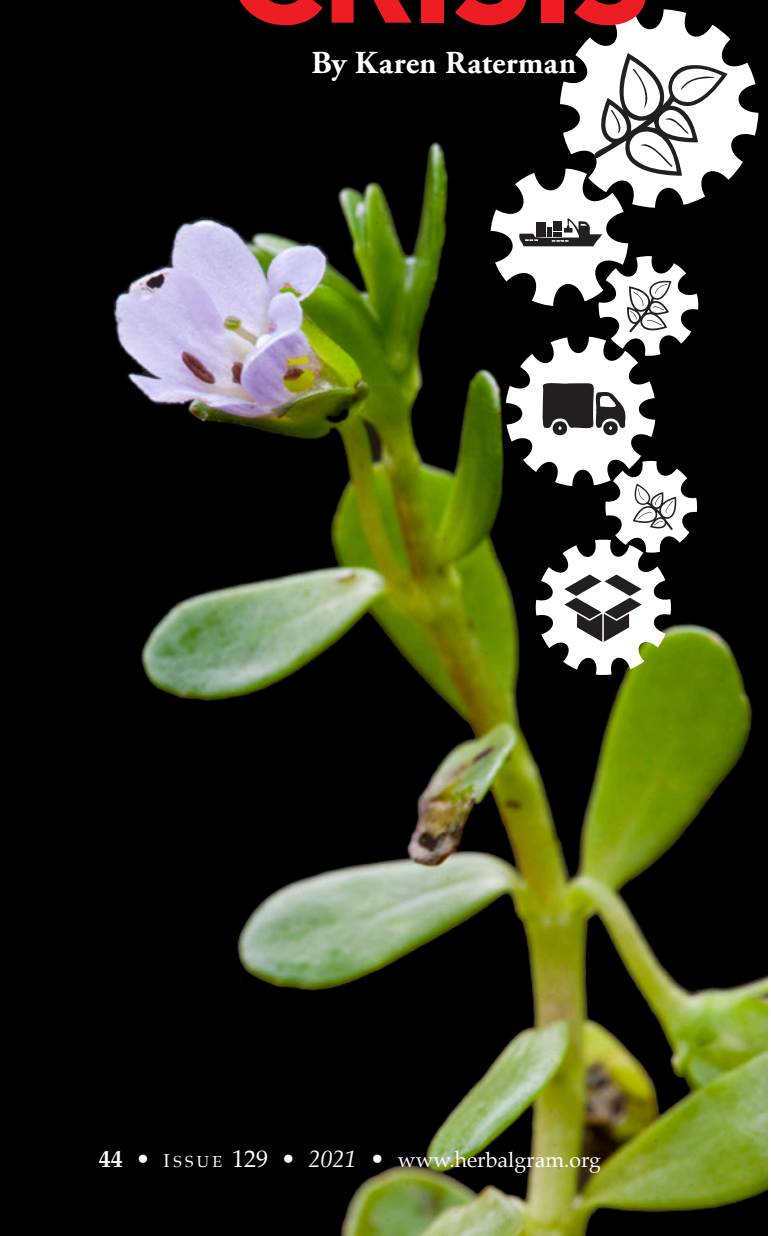
PSS scores were significantly increased at end of day in the placebo group ($P < 0.05$), but PSS scores decreased significantly in the RG and WG groups ($P < 0.0001$ for both). The RG treatment was significantly more beneficial than WG on the PSS. Adverse events were not statistically different between groups.

The authors concluded that the RG preparation was superior to WG and placebo in improving attention, memory, and perceived stress after single and repeated administration for two weeks in healthy stressed people, and RG may be beneficial as a treatment for mental fatigue. These findings may in part be due to the differences in the chemical composition between the two ginseng preparations, and the higher ginsenoside intake overall using RG. The authors acknowledge that the findings need to be confirmed with a larger population and for a longer duration. HG

In It for the LONG HAUL:

Herbal Companies Reflect on Lessons from the COVID-19 CRISIS

By Karen Raterman



***Editor's note**: This is an update of a previous article by this author, published in HerbalGram issue 126, on COVID-19-related supply chain challenges and disruptions during the first few months of 2020. This update was first published in the November 2020 issue of HerbalEGram and is based on interviews conducted in fall 2020.*

Many members of the natural products industry are reflecting on 2020 and the changes brought on by COVID-19. The pandemic has created challenges and perhaps some clarity that may not have come otherwise. Now, the questions are: What has the industry learned, and where does it go from here?

The impacts of COVID-19 have been unparalleled. Companies have faced unprecedented demand and ingredient supply shortages, ongoing logistical and transportation challenges, and pressure to adapt business practices to a rapidly evolving world while also ensuring employee safety and product quality. As companies grapple with continuing challenges and uncertainty, they also are finding better ways of doing business in this new "COVID normal." Some are building stronger relationships, developing more nimble business strategies, and looking deeper for responsible solutions to carry them forward in a time of extraordinary possibilities.

In fact, the herb and dietary supplements industries have fared better than many others, with companies in this sector being deemed essential by the US government during the early stages of the pandemic.[1] Interest in botanical health remedies is surging. In the first few months of 2020, demand increased for herbal products traditionally used for immune support, particularly in markets where traditional medical protocols like traditional Chinese medicine (TCM) and Ayurveda are prevalent, including Thailand, India, and Tunisia.[2-4] There were also reports of panic-buying of herbal products in countries like Sri Lanka.[5]

Statistics show significant increases in the use of herbal products in Western markets as well. For example, US dietary supplement sales in March 2020 were 39% higher than in March 2019, with sales still up by 14% for the four-week period ending mid-June compared to the same period in 2019, according to SPINS and *Nutrition Business Journal* data reported in the American Botanical Council's Herb Market Report in *HerbalGram* issue 127.[6] Herbal supplements commonly used for immune health saw some of the most dramatic increases during the first six months of 2020 compared to the same time period in 2019. For example, products containing elder (*Sambucus nigra*, Adoxaceae) berry, which is known for its support of upper-respiratory function,[7] saw triple-digit sales growth of 126% in the US natural channel and 241.4% in mainstream outlets in the first half of 2020.[4] Well-known immune booster echinacea (*Echinacea* spp., Asteraceae) was another big seller during this period, with natural channel growth of 70.2% and a mainstream surge of 90.9%, according to the *HerbalGram* report.

Though this is a positive development for botanical products, industry stakeholders and researchers have expressed some misgivings about the effects of this growth. It has already had significant impacts on the herbal supply chain and could have consequences on the long-term availability of plant ingredients, unless stakeholders take action to address

Bacopa *Bacopa monnieri*
Photo ©2021 Steven Foster

Licorice *Glycyrrhiza glabra*. Photo ©2021 Steven Foster

sustainable cultivation and harvesting of these plants.[8] COVID-19 cases in the United States were declining at press time for this issue of *HerbalGram* (early February 2021), but the situation remains volatile, and herb supply companies and manufacturers are working diligently to understand their vulnerabilities as they look ahead.

Then and Now

Executives in the herbal and dietary supplement space who were interviewed for this article in fall 2020 point to overall uncertainty as *the* ongoing challenge. "The impact of the early days of the pandemic [was] unprecedented, … [and we did not know] what to expect from one day to the next," wrote Ajay Patel, founder and CEO of Verdure Sciences, an Indianapolis, Indiana-based supplier of botanical extracts made in the company's factory in India (email, September 29, 2020).

For suppliers, a ripple effect started with China and other Asian countries and then moved on to Europe, North America, and South America, Patel recalled. He noted that it was "extremely challenging" to operate a business in a global economy and "navigate and adapt to the variations in national and local mandates from country to country."

Patel wrote that, comparatively speaking, "global logistics have improved significantly, although options for air freight in certain markets like India are still limited and very expensive." While supply chains have improved, Patel did express new concerns about availability and soaring prices of several key botanicals like ashwagandha (*Withania somnifera*, Solanaceae), holy basil (*Ocimum tenuiflorum*, Lamiaceae), and bacopa (*Bacopa monnieri*, Plantaginaceae), due to increased demand for these adaptogens (generally defined as herbs and fungi used to help regulate stress). "Factories, for the most part, have resumed to full operational capacity," he added. "However, we still see challenges with factory workers getting to work as a result of restrictions in communities where COVID infections are high."

Shaheen Majeed, president of Sabinsa Worldwide, had similar observations. The manufacturer, supplier, and marketer of herbal extracts, cosmeceuticals, dietary supplements, and other products, headquartered in East Windsor, New Jersey, experienced difficult logistics and labor shortages, although he noted that both have improved since the early days of the pandemic. "The labor shortages we experienced early on … are now starting to taper off, and more people are coming back to work," he wrote (email, September 24, 2020). "We did manage to keep our production going but are glad to have more people back. We are building our eighth and largest facility, which came to a complete stop for the first two months of the pandemic, but now it's getting back on track."

The stories are similar across the industry. Everything has been a learning experience, wrote Beth Lambert, CEO of Herbalist & Alchemist, a Washington, New Jersey-based manufacturer of herbal extracts and formulas for the health practitioner and natural food channel (email, September 24, 2020). "Everything was changing quickly, and everyone was just trying to wrap their heads around this new situation without much information."

Tracey Seipel, ND, CEO and head formulator of the Seipel Group, a Brisbane, Australia-based maker of herbal formulas, noted that as COVID-19 spread

around the world, down-the-line effects became difficult to anticipate and, at times, were visible only in retrospect (email, October 2, 2020).

While some of the issues faced early in the pandemic have evolved or abated, others remain. "The good news is that business is strong across the industry because people are looking for products to support their health and immune systems, in particular vitamin C, zinc, echinacea, and elder berry. Those ingredients can at times be hard to come by," said Travis Borchardt, vice president of regulatory affairs and quality control/quality assurance at Nature's Way, headquartered in Green Bay, Wisconsin (oral communication, October 7, 2020). "So, an adequate quantity of quality material may be hard to find, making the supply chain still a bit challenging. Demand in March [2020] was crazy for the whole industry. We now think of March as an extra month in the year — basically it counted for two months of demand. Even now, as supply is catching up, demand continues to be stronger than what we planned for, so we are still in catch-up mode."

Global supply regions seem to be recovering, but anticipating the future is increasingly difficult. "China has bounced back strongly since the beginning of the pandemic, and things are relatively normal," wrote Wilson Lau, vice president of Nuherbs, an Oakland, California-based importer of Chinese herbs (email, September 21, 2020). "I think the new challenge is projections — how much material will our customers, and their customers, need? We can't just turn on the spigot, which is why forecasting is important. But no one really has any good projections because we don't know what the demand will be for this winter. Will it be like March-May of [2020], slightly elevated, or even more demand?"

These problems have caused many companies to second-guess their strategies. Tal Johnson, CEO of Herb Pharm, a Williams, Oregon-based manufacturer of liquid herbal extracts, noted that isolated ingredient shortages are a part of normal business, but along with the increased demand, it was more difficult for the company to maintain the inventory buffer over summer 2020 that it prefers as it headed into the fall and winter seasons (oral communication, October 1, 2020). "We could have some challenges anticipating how much we need to prepare for and how much we should flex up for COVID."

Early on, "suppliers across the category struggled to get a clear understanding of their supply chains and potential risks, which led to material shortages and longer lead times," noted Jose Feito, divisional vice president of strategic sourcing for Pharmavite, the West Hills, California-based parent company of leading dietary supplement and herbal brands such as Nature Made® and MegaFood® (email, October 5, 2020). "Today, suppliers have adjusted to the uncertainty and have a better understanding of risk," he added. "Yet, they still continue to face challenges shoring up the supply chain to address short-term demand spikes, while at the same time, increasing lead time also presents challenges."

Tea Supply during the COVID-19 Pandemic: A Resilient but Challenging Landscape

Botanical ingredients are used in a variety of different products beyond dietary supplements and herbal extracts, and each market segment has faced specific supply chain challenges because of the COVID-19 pandemic. The tea (*Camellia sinensis*, Theaceae) industry is a case in point. Like suppliers of botanical dietary ingredients (including herbal extracts), tea ingredient suppliers also provide high-quality, dried botanicals from producers around the world. And just like in the supplement category, suppliers, brand manufacturers, and private-label packers of tea ingredients confronted many challenges in 2020, including unpredictable demand and disrupted supply channels.

The tea plant is the source of one of the most widely consumed beverages in the world, second only to packaged water.[1] Because large processors tend to hold significant inventory volumes to guard against, for example, a plant harvest failure, many suppliers had about a year's worth of inventory to meet the early spikes in demand, noted Richard Enticott, president of Boulder, Colorado-based Meridian Trading Company, which imports bulk ingredients for retail tea companies, private-label packers, and multinational coffee (*Coffea* spp., Rubiaceae) chains, like Dunkin' Donuts and Starbucks, which also sell tea (oral communication, November 18, 2020).

But the tea segment did experience uncertainty. Early in the pandemic, retail outlets like Starbucks closed. However, the good news for the tea space, Enticott said, "is that fruit and herbal tea consumption mostly happens at home. What we saw early after the March lockdown was good for business." There was some panic buying early on, he added. "Whether it was toilet paper or tea, people felt the need to stock up."

After about two months of pulling inventory forward to meet demand, Enticott said, the concern became that people would realize there would not be tea shortages and so they would drink their existing supply rather than buying more. "But that is not what we saw," he said. "People were drinking more tea than ever, even in the summer months, which are not typically big for tea consumption."

Enticott expected to see another spike in demand as parts of Europe, particularly the United Kingdom, Germany, and France, announced new lockdowns in late 2020. "These are significantly larger markets for tea than the US, so we expect demand will go up. Plus, the winter months are traditionally heavy demand months for tea."

Because larger processors maintain about a year's supply in case of localized weather issues or crop failures, high-volume tea ingredients (e.g., medicinal herbs and botanicals used for flavoring) experienced few shortages. The impact of the early spike was greater on botanicals that are wild collected. For example, Enticott explained, the harvest season for rosehips (*Rosa canina*, Rosaceae) in Chile is in February and March. "So, the trouble there is if you don't get them off the plant in time, they fall off and spoil. It is the same in the Balkan states, where a lot of medicinal botanicals come from. Getting people organized to do the collections has been the big problem," he said.

Among the variables is the number of new people trying herbal products during the pandemic and how many will continue taking these remedies. "There will be some drop in demand, and it will probably settle somewhere in between," Johnson suggested. "So, we are trying to decide what to do to build capacity temporarily [rather than] permanently."

The evolving situation has left companies confronted with a new landscape in which agility and planning are key components. "Everyone had an abrupt learning curve when the pandemic began," wrote Jim Emme, CEO of NOW Foods, a Bloomingdale, Illinois-based manufacturer of natural supplement products (email, September 21, 2020). The company has a solid system in place to safeguard the health of its team members, which is a top priority. "NOW has invested significantly in more manufacturing capacity, but it takes time to put this into operation," he wrote. "Working with vendors and contractors in this COVID-19 environment means everything is slower and more difficult."

To help manage inventory and ordering, Emme added, the company has taken care to be transparent with customers to proactively keep them informed about when specific items will be available and from which warehouse. On the raw material side, he said, supply has greatly improved, but NOW, like most of the industry, is still contending with some packaging material shortages.

Verdure's Patel sees progress regarding risk mitigation, especially as the company's business has grown with the increasing demand for several key Ayurvedic botanicals. "We've committed to expand our manufacturing footprint, both by adding new equipment to handle the growth in future demand, as well as adding new geographical locations," he wrote. Verdure has engaged with growers to expand its farmer base and plantings in certain locations to mitigate risk of varying government mandates for pandemic-related shutdowns or interruptions. "As part of sustainability initiatives, we're working with our growing communities to initiate programs for how best to support them post-COVID and the new challenges we face," he wrote.

Prioritization and backup plans for the unexpected also have become critical. "We worked with David Winston, our formulator, on what we needed to prioritize to keep in stock during the early days of COVID," Lambert recalled. "We now have very few out-of-stocks. Farmers and suppliers really responded to our requests to get more herbs to us quickly."

It is challenging, Lambert added, to establish a balance between overproducing and preparedness. She noted that the company is cautiously stocking close to its higher projection numbers and has good supplies of raw materials to work with. "Long ago, we learned that due to climate change, we had to diversify our botanical suppliers geographically as much as possible," she wrote. "This has been helpful during this time."

Looking ahead, the botanical tea supply may become more problematic, with continued high demand and less inventory buffer now available, Enticott predicted. "Growing [herbs] to produce industrial tea cannot be done overnight, so I expect we will see a very challenging 2021."

Other botanicals may also experience supply shortages, such as echinacea (*Echinacea* spp., Asteraceae), lemongrass (*Cymbopogon citratus,* Poaceae), tulsi (*Ocimum* spp., Lamiaceae), and ginger (*Zingiber officinale,* Zingiberaceae), some of which are already in high demand and popular during the cold and flu season, Enticott said.

While the tea industry has been resilient through previous crises, including economic downturns, Enticott believes there are some takeaways from 2020. "We do see companies making longer-term commitments to safeguard supply — not just because of COVID, but climate change, which is an even bigger threat."

Just changing suppliers, however, is not always a practical option. The tea industry is very sensory based, Enticott noted. "In the tea category, taste is important, so if you are used to chamomile [*Matricaria recutita*, Asteraceae] from Mexico, it would be very difficult to accept chamomile from somewhere else and accept that difference in quality and taste."

With some exceptions, the tea segment has been fortunate in its continuity of supply during the pandemic and managed to satisfy the sharp increase in retail demand for tea in 2020. The initial panic about expected supply chain interruption helped many tea companies better appreciate that they would not have a business without farmers and processors, Enticott said. After years of having a "just-in-time" approach to deliveries, companies in the segment are recognizing the value of maintaining larger inventories of botanical ingredients.

Tea *Camellia sinensis*. Photo ©2021 Steven Foster

Historically, companies that have been successful in the tea space have used marketing, storytelling, and packaging to increase the perceived value of the raw materials they use, Enticott explained. "I think they are realizing the best stories in the current market environment are the true ones about origins, farming communities, and the countless people involved in bringing these ingredients to market," he said.

Reference

1. Bolton D. Tea consumption second only to packaged water. *World Tea News*. May 1, 2018. Available at: https://worldteanews.com/tea-industry-news-and-features/tea-consumption-second-only-to-packaged-water. Accessed November 18, 2020.

Amla *Phyllanthus emblica*. Photo ©2021 Steven Foster

As companies grapple with continuing challenges and uncertainty, they also are finding better ways of doing business in this new "COVID normal."

Before the predicted fall and winter wave of the pandemic, many companies were shoring up procedures in the workplace; continuing to work at home; bolstering projections for immune support, stress, and adaptogen products; and ensuring adequate supply, processing, and packing materials.

For example, Green Bay, where Nature's Way is headquartered, was, in mid-October 2020, labeled a COVID hot spot.[9] "So we are already in the second wave," Borchardt said at the time. "We have been operating all along as if this is not a short-term pandemic, but will last a while, and so we must design a work practice and relationships and a supply chain with the thought that this will go on for some time."

Given the rise in cases and the strain on local hospitals in the Green Bay area at the time, Borchardt said the company was working to ensure safety but also to continue to supply its products. "One thing we take very seriously is the ability to positively impact lives and health of people during this time. So, we have strict policies on social distancing, personal protective equipment, and employees entering healthy without symptoms. Our mission is to continue to provide products to the market."

Persistent Problems

While preparing for the future has been a priority for many companies, other challenges have also represented a persistent grind. For most industry companies, whether they use internal manufacturing facilities or contract manufacturers, the available human resources and manufacturing capacity have impacted industry operations and production. Keeping people safe is the top priority.

Johnson noted that, early on, Herb Pharm was primarily concerned "about staying in operation and continuing to make anything in a pandemic. It was not whether we could get more supply or make enough, it was 'can we operate in this environment?'"

"Overnight, we became public health officers with no training," he added. This meant many late-night phone meetings, researching information from the Oregon Health Authority, networking with peers, and sharing protocols. "Many companies shared information with us, so there was a huge spirit of helping. People let down their guard, in our experience, and shared the work we were all doing to help us get up to speed and get better faster. One large company loaned us their company doctor to help us with protocols and [offered] many suggestions," Johnson said.

Keeping employees safe has required many new procedures for suppliers and manufacturers around the world, including rigorous cleaning and sanitizing procedures, health screenings and daily temperature checks, and use of protective masks and social distancing policies. For Nature's Way, these modifications impacted business operations, Borchardt noted. The strict social distancing between people in the

factory, he said, led to reduced capacity and product in the face of higher demand, as well as some reduced service levels. "We've done the best we can to keep up while also managing our business and manufacturing facility in a way that says, 'safety first.' And we are continuing to do this," he added.

Sabinsa also took serious measures to reduce the chance of infection and provide peace of mind in the workplace, all of which are still in place, Majeed noted. "The temperature of each employee is monitored every day before reporting to their workstations. The company has installed additional handwashing facilities and implemented other increased sanitation practices. Regular health check-ups are being conducted … to identify any infections early on to minimize the potential for virus transmission to others."

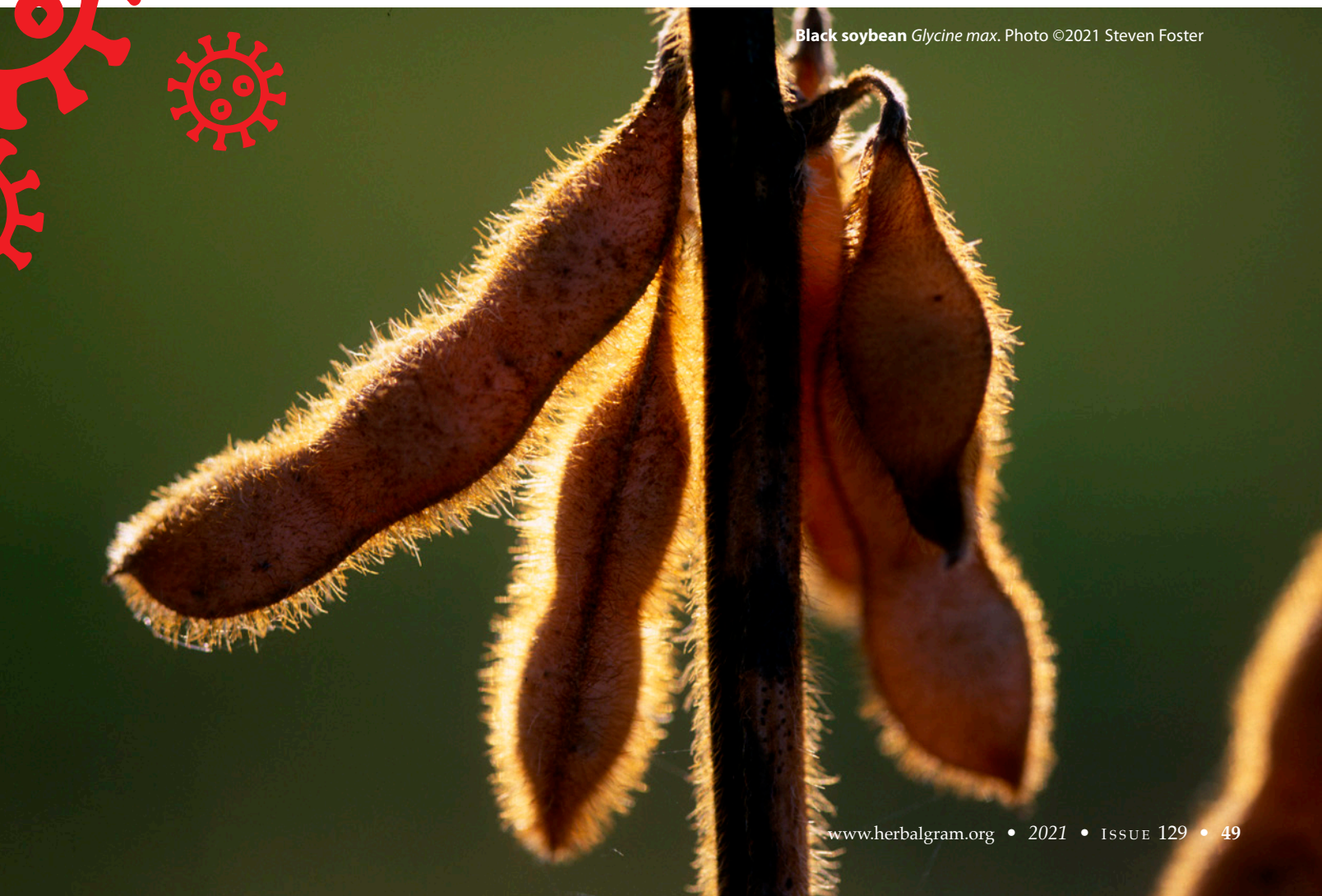
Many companies anticipate that these procedures will be necessary for a while yet. "I do [anticipate] some of these being in effect for the long term or permanently, especially work-from-home or hybrid roles," said Scott Benedict, vice president of supply chain operations of the Manchester, New Hampshire-based brand MegaFood (email, September 23, 2020). "I expect us to keep up with the additional cleaning and sanitizing protocols. I would like to see masks and social distancing relax once a vaccine is available and the threat of this subsides."

Many Herb Pharm employees began working remotely early on and many still are, Johnson noted. "We improved our network infrastructure, bought a lot of laptops, and started using Microsoft Teams, which has been very helpful in the long run," Johnson said. The company also made some physical changes in its facilities, such as relocating the shipping department to another building, to better enable social distancing.

Herb Pharm also made free flu shots available to all staff in September 2020 and installed high-efficiency particulate air (HEPA) filters throughout its facilities. The company anticipated some employees would develop flu-like symptoms in the fall and winter, and providing flu shots "would help reduce the number of false alarms," Johnson explained. The HEPA filters, he added, give no guarantee, but represent an additional measure of protection. They were also beneficial because Williams was near the late-summer wildfires in southern Oregon, and the filters helped reduce the amount of smoke indoors, which allowed the facility to keep running during the worst of the fires.

Beyond making physical changes, it also has been important to communicate the reasons for the changes, Johnson explained. "These protocols are very [difficult] to maintain and very expensive, so we had to help [employees] understand why we were doing what we were doing to help them feel safe."

It was important for Herb Pharm to safely limit disruptions so it could stay in operation. Because the company is the largest employer in Williams, this was crucial for the community, especially as the wildfires further impacted the



Black soybean *Glycine max*. Photo ©2021 Steven Foster

region. People who need to quarantine can still work while in isolation, Johnson noted. "It takes everyone in the company following the protocols and understanding why they protect our ability to make [products]. Having that culture is important."

Changes in human resources have been prevalent throughout the supply chain and have required herbal companies to be more diligent to ensure proper herb identification and quality. "We have seen human error in areas that would have been extremely unlikely prior to the pandemic," noted Seipel.

Seipel experienced an issue with material from a US warehouse that was short-staffed. "The warehouse could only have one employee in attendance, so the logistics manager was performing the role of the warehouse manager. They sent material to us that looked like it was correct to the logistics manager, except that it was the wrong plant part. It is these human errors that [may] not have happened pre-pandemic when all staff was working. Of course, it was detected at the next step and resolved, but it all adds further delays to our production," she said.

The lack of human resources has had other impacts. For example, the pandemic delayed issuance of Native Plant Harvesting Permits for saw palmetto (*Serenoa repens*, Arecaceae) fruit by the Florida Department of Agriculture, as their offices closed and their staff worked from home, according to Guy Woodman, US-based general manager of Euromed S.A., a producer of standardized herbal extracts based in Barcelona, Spain (email, September 28, 2020). In addition, he said, banks in Florida were closed, reducing access to cash needed to purchase saw palmetto fruit.

Lockdowns and Logistics

Lockdown orders have impacted both interstate transportation and international shipping, with limitations on air and sea vessels and the closure or reduction of operations of ports. While some of these issues have improved, they are still challenging, especially for suppliers.

"Logistics and transportation remain the biggest challenge for [Sabinsa] during the pandemic," wrote Majeed. "When India first went into lockdown, interstate transportation was closed off for several weeks. Each state had to act independently to meet the state population's needs for food and everything else, for some time." This was problematic for Sabinsa because much of its turmeric (*Curcuma longa*, Zingiberaceae) processing takes place in the southwestern state of Karnataka, but the turmeric raw material itself is largely from the state of Tamil Nadu, located on the southeastern coast of the subcontinent.

Some of these issues, Majeed explained, were resolved as the Indian government recognized "essential" businesses and granted permits for vehicles to cross state lines. Migrant workers were also hit hard during this time, and most had no choice but to return home to their villages, causing shortages of labor everywhere in India, Majeed recalled.

Even as some of these challenges eased, others took their place. Shipping prices increased, Majeed noted, but Sabinsa prioritized getting deliveries to customers during the early high-demand days of March and April 2020 and did not pass these costs along.

Ettore Milano, director of procurement for Indena SpA in Milan, noted that increasing sales of ingredients for immune health, which surpassed demand for other products, "created challenges with some of our raw material (biomass) suppliers," he wrote, adding that he expected the trend to continue in 2021 — even with a vaccine (email, September 22, 2020).

Finished product manufacturers are changing their product development patterns, with some companies using approved ingredients to expand their pipelines and meet consumer demand or rapidly expanding their product portfolios with new offerings, Verdure's Patel wrote.

Clinical trials and other research were also disrupted when some research organizations, medical centers, and universities either closed or focused on COVID-19 research. "Euromed has experienced delays in clinical studies for new products that were in development," wrote Woodman. "The COVID outbreak has disrupted recruitment and participation of subjects for clinical trials, delaying new product introduction."

Understanding the Supply Crisis

High demand, especially for immune-support ingredients, and logistical and labor issues have highlighted vulnerabilities — and the overall resilience — of the herbal ingredient supply. Many companies predict these issues are likely to continue for the foreseeable future and will have an ongoing impact on raw material prices, product development, quality, and the potential long-term availability of certain medicinal and aromatic plants.

Growing evidence suggests that some of these medicinal plants may be of value for treating COVID-19. According to a June 2020 report called "The Invisible Trade: Wild Plants and You in the Times of COVID-19 and the Essential Journey Towards Sustainability," from TRAFFIC, a wildlife trade monitoring network, a combination of TCM and Western treatments were used in China to treat COVID-19 patients with varying levels of success. An official COVID-19 treatment protocol issued by the National Health Commission of the People's Republic of China included 10 TCM formulations and 13 proprietary Chinese medicine formulations.[8] More than 125 specific plants are used in these formulations, according to the TRAFFIC report, including licorice (*Glycyrrhiza* spp., Fabaceae) root, Asian ginseng (*Panax ginseng*, Araliaceae) root, and magnolia (*Magnolia officinalis*, Magnoliaceae), and many of them are protected either in China and/or listed in CITES Appendix II, which includes species that are not currently threatened with extinction but may become so without trade controls.[10]

For now, availability of Chinese herbs seems to have normalized. Subhuti Dharmananda, PhD, founder and director of the Institute for Traditional Medicine in Portland, Oregon, noted that March through May 2020 saw a depletion of Chinese herb supplies in the United States (email, September 9, 2020). Dharmananda noticed low summer availability of the Asian herb andrographis (*chuan xin lian*; *Andrographis paniculata*, Acanthaceae), for example, which has been shown to have antiviral properties.

"There remains a high demand in the US for Chinese herb formulas that are deemed immune enhancing or antiviral or [beneficial for] treating lung disorders, and some companies

Echinacea *Echinacea angustifolia*
Photo ©2021 Steven Foster

Stevia *Stevia rebaudiana*
Photo ©2021 Steven Foster

Black rice *Oryza sativa*
Photo ©2021 Steven Foster

Ashwagandha *Withania somnifera*
Photos ©2021 Steven Foster

have come out with prepared forms of formulas mentioned in reports as being used in China for [COVID-19]," Dharmananda wrote.

Other herbal ingredients and formulas also are seeing interest. Sabinsa, Majeed wrote, saw high demand for ingredients including curcuminoids from turmeric rhizome extract, amla (*Phyllanthus emblica*, Phyllanthaceae) fruit extract, andrographis leaf extract, ashwagandha, frankincense (*Boswellia serrata*, Burseraceae) gum extract, ginger (*Zingiber officinale*, Zingiberaceae) rhizome extract, holy basil/tulsi extract, rosemary (*Rosmarinus officinalis*, Lamiaceae) leaf extract, and spirulina (*Arthrospira platensis*, Microcoleaceae) extract, as well as various vitamins and minerals.

It has been a big challenge, Verdure's Patel wrote, "to get consistency in the quality of raw botanicals, which we use to produce our standardized extracts. In addition, due to increases in demand for several botanicals [at the beginning] of the pandemic, coupled with the pandemic-related harvesting and logistical challenges, we've seen a steep increase in cost of several key botanicals like ashwagandha, holy basil, bacopa, and tinospora [*Tinospora cordifolia*, Menispermaceae]."

Similarly, Gaia Herbs faced a large spike in sales for its immune-related products, which stressed its supply chain early, wrote Chase Millhollen, global sourcing manager for the Brevard, North Carolina-based herbal formula manufacturer (email, October 2, 2020). The company, he noted, experienced ongoing shortages of *Echinacea angustifolia* and *E. purpurea* root because of the massive global demand. "Even though we grow echinacea on the Gaia Farm, we must also work with key partners to keep up with demand, as we currently cannot grow the quantity needed for all our products with just the yield from our fields," he wrote. "Since our biomarker specification for these echinacea varieties is very high to produce a therapeutic finished product, it has been challenging to find enough suppliers that can meet these stringent standards."

These shortages, he added, have prompted some out-of-stocks and backorders for Gaia's echinacea-based products, because the company would rather be out of a product than use inferior ingredients. "Fortunately, the harvest for echinacea root is just around the corner, and we expect the situation to greatly improve as we harvest from both the Gaia Farm and procure additional material from our trusted partners in North America and Europe," Millhollen wrote.

Availability of these plants and logistical issues in some countries are leading many companies to seek new supplier partners. The situation in India has prompted Gaia to pursue ingredients in other parts of the world that have similar climates and can grow the same herbs, such as South America. "This risk mitigation practice was already part of our supply chain risk assessment before COVID, but it is now an even bigger focus during the pandemic and beyond," Millhollen wrote. For example, the company will now source critical supplies of turmeric not only from India, but also Indonesia and Nicaragua to ensure reliable sources for its Turmeric Supreme® line.

Adulteration and Other Concerns

With supply chain issues around the world and ongoing shortages, many companies are concerned about adulteration. As the largest brand holder of an elder berry product, Nature's Way has been particularly concerned about elder berry raw material. "[W]e have had significant out-of-stocks due to unplanned demand," Borchardt said. "That is where we have seen challenges around quality and testing that we have done."

As part of an effort to find additional elder berry supply, Nature's Way tested 25 bulk elder berry extracts and eight finished products available in the market and released concerning results in September 2020.[11] Borchardt explained that the company developed specific methods to detect *Sambucus nigra*, the European elder berry species used in the Nature's Way product, as well as another method to detect other anthocyanins that might be added to impact a product's potency, such as from black rice (*Oryza sativa*, Poaceae), black soybean (*Glycine max*, Fabaceae), and blueberry (*Vaccinium* spp., Ericaceae).

"Once we developed these methods, we tested 25 sources and found that about half were adulterated, containing sources of anthocyanins other than from elder berry — 20% actually contained no elder berry at all. So, this is a very concerning set of findings," Borchardt said, adding that the most common adulterant was black rice.

These concerns are well founded, according to Elan Sudberg, CEO of Alkemist Labs in Garden Grove, California, writing in an August 2020 blog post. He noted that "as supply chains are strained and compromised, the frequency of testing is up, which speaks to the wisdom and integrity of our clients. Perhaps unsurprisingly, though, given the unprecedented circumstances, we have noticed some emerging trends and the failure rate is on the rise."[12]

Sudberg provided a list of 29 botanicals that are failing more consistently than normal. Other than the herbs previously noted as in short supply, Alkemist's list includes barberry (*Berberis aristata,* Berberidaceae), cannabis (*Cannabis sativa*, Cannabaceae), garcinia (*Garcinia cambogia*, Clusiaceae), garlic (*Allium sativum*, Amaryllidaceae), red clover (*Trifolium pratense*, Fabaceae), and stevia (*Stevia rebaudiana*, Asteraceae).

The demand may not only affect cultivated botanicals but also lead to overharvesting of wild plants. "As medicinal plants receive increased scientific and commercial attention, there is increasing pressure on the wild plant populations from which many medicinal plants are harvested," wrote Majeed. He noted that a good example is Indian kino tree (*Pterocarpus marsupium*, Fabaceae) heartwood, which has been shown to support healthy blood sugar levels and is extracted from trees grown for more than 30 to 40 years. As modern research validates the traditional uses of these plants, growing demand leads to increased harvesting.[13]

"We began a pioneering reforestation program for this species several years ago, but that's just one botanical," Majeed wrote. "Overharvesting has placed many medicinal species at risk of extinction. Commercial exploitation has also sometimes led to traditional medicines becoming unavailable to the indigenous peoples that have relied on them for millennia."

The time for suppliers to act is now, Majeed added, citing that boswellia, or Indian frankincense, the resin from the *B. serrata* tree, is under increasing pressure, so planting boswellia trees is now a priority. He added that ashwagandha supply is also strained and suggested that large-scale cultivation should be taken up by private companies to ensure global demands are met.

Extra Due Diligence

"In times of high demand for certain herbal materials, there is always a risk of getting substandard raw materials," Majeed reiterated. "However, our screening and [quality control] team are well trained to protect us, and our customers, from this happening with any Sabinsa products."

Although they do not have confirmed reports of adulteration, Verdure is concerned about the increases in demand for botanicals sourced in India, such as ashwagandha, holy basil, shatavari (*Asparagus racemosus*, Asparagaceae), and tinospora. "We are closely following these trends and being extra cautious with our purchase of these botanicals," Patel explained.

Nuherbs' Lau wrote: "We are constantly monitoring ingredient purity to ensure that our ingredients are not adulterated. Our systems are quite robust and we are confident in our ability to ensure identity, quality, and purity of all of our materials."

Rosehip *Rosa canina*
Photos ©2021 Steven Foster

Lau added that Nuherbs is constantly learning and looking for ways to improve its systems. "Adulteration is like a living evolving being, with people constantly trying new things to fool customers, so you have to be constantly learning and keeping vigilant," he wrote.

Euromed's Woodman echoed that thought. "Producers of adulterated botanical extracts have become more sophisticated in their mixing of species and addition of synthetic compounds to emulate the natural product," he said. "This requires a level of analytical expertise not present at typical US contract laboratories. As pricing pressure on … herbal raw materials has increased, and subsequently the price of standardized extracts, the attractiveness of adulterated lower-cost extracts has increased."

There also is concern within the industry that adulteration could escalate as the products remain in the spotlight. "We are seeing the dietary supplement category, from a business perspective, continue to be attractive," said Borchardt. "The pandemic opened the eyes of consumers who prior to the pandemic were not participating in the category…. With increased business opportunity comes the risk of opportunistic players — those looking to take advantage of the category … by selling [inferior products]."

Furthermore, vetting of suppliers and even US Food and Drug Administration (FDA) inspections often

are being done virtually to protect the health of workers and inspectors. This, Sudberg wrote, is like giving adulterators a free pass.[11]

Though the challenges are significant, they also present opportunities for the industry to reflect, learn, and mature. "I am always concerned when there is change, and especially when you weren't prepared for it," wrote Lau. "However, the digital tools that we have access to today have helped overcome a lot of problems. We know [our suppliers] and their facilities well, so for us it is less of an issue than for [companies] that had to bring in new vendors under virtual inspections."

According to Gaia's Millhollen, before the pandemic, his team regularly visited the farms, fields, and even local communities to see how everything is done, make sure that positive business practices are followed, and look for suppliers that adhere to environmentally and socially responsible business practices and natural resource conservation.

"[In 2020], due to the pandemic, our sourcing team [was] not able to travel to do these in-person inspections," Millhollen wrote, adding that this is where long-standing relationships with trusted suppliers become even more important. "To become an approved Gaia Herbs supplier, a company or farmer must go through a rigorous qualification process where we test initial batches of herbs to ensure the material's safety and potency. In addition, Gaia Herbs has created our own DNA-validated botanical reference library that we use to confirm identity of our raw materials, and all materials … must meet our strength claims, such as biomarkers, and also meet our specifications for pesticides, microbes, and heavy metals."

Even though Gaia Herbs works with long-term suppliers, the company still verifies every ingredient used and shares the results at meetyourherbs.com, an herb traceability platform.

Such programs take time, commitment, and investment. Over the years, Patel wrote, Verdure has emphasized the chain of custody, which "is a complex process and involves the development of validated analytical tools, investment in analytical instruments, technical expertise, agricultural programs, and establishment of a reliable grower/supplier base for raw botanicals, with intrinsic focus on sustainable initiatives. Additionally, as the industry evolves and matures, so must we, and we must be willing to embrace the sheer challenges of not only events such as the COVID-19 pandemic, but also climate change and sustainability."

More recently, Verdure has put more focus on mitigation and maintenance of its supply chain with dedicated teams to oversee compliance of not only its manufacturers, but also all aspects of its supply chain. "Most importantly, in this new COVID era, we've enhanced our supply chain oversight via virtual audits as frequently as on a weekly basis," Patel wrote.

Ramping up Resilience

The good news, according to Millhollen, "is that problems that have always been in the supply chain have now been brought to the surface and are being analyzed and corrected."

However, the answers are not clear cut and many issues should be considered, such as changing weather and environmental conditions and their impacts on crop performance and quality, as well as the evolving global trade situation and variable relationships with specific supplier markets, all of which might make the case for more and varied supply. However, said MegaFood's Benedict, too much variety is not always good. "You end up with a lot of products with very small amounts of lots of ingredients."

It is likely that solutions will require both individual company foresight and broad industry coalition.

Gaia Herbs is looking at how to improve the variety and resilience of its North American supply. "With continued international supply chain issues, dual sourcing has become even more important," Millhollen wrote. "Our goal is to try and dual source all of our key herbal ingredients. We look for multiple suppliers from different parts of the world and prioritize trying to find a North American source as one of our approved vendor options."

This strategy, Millhollen explained, helps minimize risk in the supply chain, especially if there is a bad harvest in one part of the world and one of the company's suppliers cannot produce the supply of materials needed. "It also helps when dealing with a situation like the current COVID pandemic, where there have been government lockdowns in other countries causing lengthy shipping delays, so having a North American supplier option may be critical to getting the ingredients needed to keep products on the shelf," he said.

"The negative is that sourcing from multiple vendors from around the world typically comes with increased costs," Millhollen added. "However, we have been willing to accept these increases to build stronger variety and resilience into our supply chain."

Lau added: "I think we can increase our inventories as an industry to create a buffer against issues in the supply chain, whether that be a pandemic or some other natural disaster. We need to work with each other in a collaborative fashion, so we can build in buffers, grow or source enough material, and move away from just-in-time ordering, which seems more capital efficient but [can lead] to out-of-stock situations."

Lessons Learned

The herbal products and dietary supplements industries were fortunate in 2020, despite many challenges. Gaining a better understanding of the supply chain, becoming more open to broad collaborations, and working differently and more efficiently are just a few examples of the how the industries progressed in 2020.

"During what has been an unprecedented year for all manufacturers, we have gained a much deeper understanding of second- and third-tier supply chains," wrote Pharmavite's Feito. "In addition, we are collaborating more closely with our suppliers, which has been critical to ensure our supply. For instance, we are providing sourcing assistance to support our supply partners and contract manufacturers."

A top takeaway for Milano at Indena is that companies with strong organizational models perform well even in difficult times. "The other important message is that customers' education on the quality of products is very important as the visibility of single ingredients is [increasing]."

Patel added: "The onset of the pandemic has reminded us of the importance of supply chain alignment and mitigation and the impact of climate change, which has been more evident in recent years than ever before. This, coupled with the [projected] post-pandemic growth of our industry, signifies

the need for checks and balances across our supply chains and is also a reminder to brand owners that continuous investment and support in ingredient supply partners is necessary to ensure growth and sustainability of the industry as a whole."

Companies are working smartly and using technology more efficiently, but most are also realistic. "We are all in the same boat, and we have all had to appreciate that some delays are unavoidable," wrote Seipel. "My experience is that open and frank communication is essential, and the result is we have an even better working relationship with our suppliers, manufacturers, and business partners."

"We have a great team that has done some amazing things to help keep us connected as coworkers," Benedict added. "A big challenge that has not been overcome yet is the sales force returning to the field and having direct connections with customers and retailers. We have seen a significant uptick in our direct-to-consumer business as consumers will come directly to us looking for product if retailers are out of stock and also, more consumers are shopping from home."

Though the business environment may have been irrevocably altered, there are also reasons to be optimistic. More than 80% of the Nature's Way team is now working from home and lack of face time initially was a concern, but the company equipped staff to work effectively at home. "We've learned we don't need to be face to face or in the same office to work effectively," said Borchardt. "And now people get more quality time with family and kids and have the flexibility to log in and log out as needed."

Red clover *Trifolium pratense*
Photos ©2021 Steven Foster

Nature's Way also has increased its efforts to assist its community in these tough times. In the Green Bay area, the company is sponsoring meals for children who are not getting school meals and care packages for health care workers. "Our industry has been fortunate in that we have stayed open, and we are thriving," Borchardt said.

Ultimately, for most herbalists it comes back to the mission. "It's been interesting and kind of wonderful to experience how many people immediately turned to herbs to keep themselves healthy when a medical crisis hit," wrote Herbalist & Alchemist's Lambert. "And it's been gratifying to provide products that meet that need."

The biggest thing for Herb Pharm, Johnson said, has been protecting the health of their employees, especially vulnerable employees. "The idea that someone might get sick because they come to work is not acceptable. Our measures were designed to prevent and protect against that and protect jobs and operations so people can take care of their families and stay healthy. That is what we've worked on, in that order and priority." HG

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THE ETHNOBOTANY of WINE as MEDICINE IN THE ANCIENT MEDITERRANEAN WORLD

By Mark Plotkin, PhD, LHD

"Wine [is] one of the oldest, perhaps the oldest, of all medicines."

–S.P. Lucia, MD (1963)

Wine is not only one of humankind's most ancient drinks, it also may be the first recorded medicine.[1] It is not merely a beverage but has served as an analgesic, antiseptic, menstruum (solvent), soporific (sedative), valuable economic commodity, water purifier, social lubricant, and even an inspiration. Wine is, for some, the ultimate creative juice. In fact, this author proposes that wine, and the wine grape (*Vitis* spp., Vitaceae) from which it is prepared, has played a greater role in the evolution of human society than any plant other than cereal grains.

Many people associate the beginnings of wine culture with the Greeks and Romans of the ancient Mediterranean world. However, this is incorrect, both biologically and historically. "Catching a buzz" from alcohol from fermented fruits did not originate with the Greco-Roman world of 2,000 years ago and did not even begin with our own species. Alcohol consumption presumably predates the emergence of *Homo sapiens* by millions of years, since fermented fruits are known to be consumed by insects like bees, butterflies, and fruit flies, birds like cedar waxwings and robins, and mammals as diverse as bats, chimpanzees, elephants, howler monkeys, and tree shrews.[2,3] Undoubtedly, a complete list of animals that experience altered states induced by alcohol from fermented fruit would be much longer.

Figure 1. Notable Locations in the History of Wine

Map courtesy of Brian Hettler and Rudo Kemper (Amazon Conservation Team).

Viniculture in Transcaucasia

While the fermentation of sugars from many sources can yield an alcoholic drink, this article focuses on wine derived from the common wine grape, *Vitis vinifera*, whose original range covered much of Eurasia. Ancient humans may have been consuming naturally fermented grape juice throughout this range for many thousands of years. But archaeological evidence clearly points to Transcaucasia — a region roughly comprising the present-day countries of Armenia, Azerbaijan, and Georgia and parts of both Iran and Turkey — as the place where humans began to purposefully and systemically plant grapes and process them into wine.[4] The oldest known extant proof of wine production is pottery shards of vats that once held wine and were excavated in the Republic of Georgia by Patrick McGovern, PhD, of the Penn Museum and a leading authority on the production of wine in the ancient world. McGovern and his colleagues date the production of this wine to around 8000 BCE. Other jars used for wine storage were found at the Hajji Firuz Tepe archaeological site in northwestern Iran and dated to approximately 5000 BCE.[2]

In *Uncorking the Past* (University of California Press, 2009), McGovern writes:

> It is also becoming increasingly clear … that the world's first wine culture — one in which viniculture, comprising both viticulture and winemaking, came to dominate the economy, religion, and society as a whole — emerged in this upland area by at least 7000 BCE.[2]

Interestingly, the wine residues found at this Iranian site contained a plant resin from the terebinth tree (*Pistacia terebinthus*, Anacardiaceae). Plants from the genus *Pistacia* appear repeatedly in the Bible. Terebinth resin was valued for its preservative properties and was used by the Egyptians in the mummification process.[5] A major challenge for winemakers has always been to keep bacteria from converting the alcohol to vinegar. Though they could not have understood the underlying processes, the winemakers in this region likely were using this natural product to kill unwanted microorganisms, a practice that anticipates the research of Louis Pasteur and Alexander Fleming that revolutionized medicine almost 7,000 years later.[6]

Evidence of the most ancient winery known, believed to be in use as early as 4000 BCE, was found in the Areni-1 cave complex in central Armenia. This site yielded not just pottery shards but also cups, fermentation vats, storage jars, and a wine press. In the words of McGovern: "The fact that winemaking was so well developed in 4000 BCE suggests that the technology probably goes back much earlier."[7]

Why wine cultivation evidently began in the Transcaucasus region remains unknown. Transcaucasia is bracketed by two seas, the Black Sea to the west and the Caspian Sea to the east, and was a crossroads of trade and culture. The legend of Jason and the Golden Fleece, which recounts the Argonauts' sailing east from Greece to the land of Colchis (modern-day Georgia), most likely represents a retelling of the Greeks' initial meeting with the people living on the east coast of the Black Sea and coming away possibly with the Golden Fleece, but in all probability with new grape cultivars and additional knowledge as to how to best cultivate grapes and process them into wine.[8]

Wine amphora.
The Hasanlu Project (Hajji Firuz Tepe); Mary M. Voight, 1969.
5400-5000 BCE. Image courtesy of the Penn Museum.

The first known representation of wine appears on the Standard of Ur, an ancient Sumerian box with inlaid stones. 2600–2400 BCE. Photo ©2021 Frans Vandewalle

A Symbol of Wealth in Mesopotamia

The history of wine and viniculture does not move directly from Georgia to Greece. Ironically, wine next appears in the historical record where the wine grape did not thrive — in the hot and dry deserts of Mesopotamia. In fact, the first known depiction of wine drinking is featured on a Sumerian box dated to 2600-2400 BCE. The artwork, known as the "Standard of Ur" and now on display at the British Museum, portrays a king seated on a carved stool while being toasted by six attendees holding wine cups.[9] Wine, which had to be transported from far away, was the preferred drink of royalty because it was safer and tastier to drink than much of the available water, it induced altered states, and it could be used for curative purposes.

King Ashurnasirpal II of Assyria (reign: 883–859 BCE) is said to have invited almost 70,000 guests to a feast to celebrate the completion of his new palace at Nimrud in 870 BCE. According to Tom Standage in his classic *A History of the World in 6 Glasses* (Bloomsbury Publishing, 2005):

> [He] served ten thousand skins of wine — [an] impressive display of wealth. Previously, wine had only been available in Mesopotamia in very small quantities, since it had to be imported from the mountainous, wine-growing lands to the northeast. The cost of transporting wine down from the mountains to the plains made it at least ten times more expensive than beer, so it was regarded as an exotic foreign drink in Mesopotamian culture. Accordingly, only the elite could afford to drink it, and its main use was religious; its scarcity and high price made it worthy for the gods, when it was available. Most people never tasted it at all.[10]

McGovern echoes Standage's analysis that wine became the drink of royalty in Mesopotamia because, unlike in the Caucasus, it required massive labor and expense to be produced in a challenging environment: "Wine belonged to a different social order in lowland Mesopotamia … where grapes could be grown only by irrigation and had to be protected [from] the intense sun. Only royalty could afford to indulge in this luxury."[2]

Early Evidence of Wine as Medicine

Meanwhile, the earliest known record of wine used as medicine also comes from ancient Sumer. A cuneiform tablet from the ancient city of Nippur in the Iraqi desert, dated to about 2200 BCE, features what is widely regarded as the world's oldest medical prescription, suggesting that the use of wine for medical purposes is likely as ancient as wine itself. Not only is wine our oldest documented medicine, it is also our oldest man-made medicine.

The tablet contains detailed accounts of various prescriptions, many consisting of salves created from crushed medicaments, some of which are then infused with wine.[11] One translated prescription appears in Lucia's 1963 book, *A History of Wine as Therapy* (J.B. Lippincott & Co.): "Pound together: dried wine dregs, juniper and prunes, pour beer on the mixture. Then rub [the diseased part] with oil, and bind on [as a plaster]."[1]

Though the disease being treated is not specified, the external application of the mixture as a plaster probably indicates that it is a wound or infection. The alcohol in the beer[a] that was poured onto the mixture may have had a mild antibacterial effect; the Sumerians were passionate about beer and brewed many different varieties. More important from a

[a] Beer is generally believed to have been produced initially in Mesopotamia. For the purposes of this article, beer is defined as alcohol produced by the fermentation of sugar from starches (originally derived from barley [*Hordeum vulgare*, Poaceae] or wheat [*Triticum aestivum*, Poaceae]), whereas wine is alcohol produced from the fermentation of sugar from fruit (in this case, grapes).[12]

therapeutic standpoint, however, was the wine: grape wine has been proven to contain several antibiotic compounds.

Famous in the annals of medical history is English physician John Snow's (1813–1858) study of the 1854 Broad Street cholera outbreak in London, which led to the understanding that cholera can be transmitted through contaminated water. Less widely celebrated was an 1892 paper by the Austrian military physician Alois Pick (1859–1945) that constituted the first known scientific demonstration of wine's antiseptic properties. Like Snow four decades before him, Pick noticed who did — and more importantly, who did not — get sick during a cholera epidemic, this time in Paris. Noting that wine drinkers did not contract the deadly disease, Pick carried out a simple experiment. He mixed both cholera and typhoid bacteria with wine and observed that the microbes expired, leading to many subsequent experiments that yielded similar results and conclusions.[11] Guido Majno, MD, in his book *The Healing Hand* (Harvard University Press, 1975), notes:

> The antiseptic power of wine is no myth…. Since it cannot depend on alcohol alone … [recent research has pinned] down the mechanism to the anthocyanes, a subgroup in the large group of polyphenols present in wine. The most important member of this group of compounds, as regards antibacterial effects, is also the principal pigment of red wines, malvoside or oenoside; there is a colorless equivalent for white wines. This pigment is already present in grapes, but combined with a carbohydrate and not antiseptic; during alcoholic fermentation it splits free and becomes activated.[11]

Thus, observations in Paris at the end of the 19th century confirmed the effectiveness of wine as an antibacterial, a property ancient people took advantage of more than 4,000 years ago, and likely far earlier than that.

Wine in Canaan and Mediterranean Trade

From Mesopotamia, wine culture moved west to the land of Canaan. The Canaanites were Semitic peoples who inhabited much of the ancient Near East. Canaan itself usually refers to Lebanon, and portions of present-day Israel, Palestine, and Syria.

Lebanon in particular, with its greater precipitation, higher elevation, and better soils, proved ideal for viticulture compared to the flat, parched, and sandy landscapes of much of Mesopotamia. A group of enterprising Canaanites from coastal cities like Byblos, Sidon, and Tyre, as well as the fertile Beqaa Valley to the east, developed an extraordinary maritime culture focused on trade rather than conquest. These coastal Canaanites later became known as the Phoenicians and appear in ancient sources as varied as Egyptian tomb paintings, Homer, Herodotus (ca. 485–424 BCE), and the Bible. (The Phoenicians flourished from approximately 1200 BCE to 539 BCE.)[4]

Three ethnobiological products — two botanical, the other zoological — played fundamental roles in the Phoenicians' mastery of Mediterranean trade. The cedars of Lebanon (*Cedrus libani,* Pinaceae) were once the largest and most majestic trees in the region now known as the Middle East. They also produce a magnificent wood: beautiful, easy to work, fragrant, and decay resistant. The cedar enabled the Phoenicians to build the biggest and strongest ships of the day, so for the first time in Mediterranean

A cuneiform tablet from the ancient city of Nippur in the Iraqi desert, dated to about 2200 BCE, features what is widely regarded as the world's oldest medical prescription, suggesting that the use of wine for medical purposes is likely as ancient as wine itself.

Medical tablet found at Nippur, dated to ca. 2200 BCE. Photo ©2021 Jose R. Valverde

A Roman wine amphora dated to ca. 100 BCE. This terracotta jug was among more than 1,000 amphorae found by Capt. Jacques Cousteau and Prof. Fernand Benoît in the Grand Congloué shipwreck off the coast of France in the early 1950s. Image courtesy of The Metropolitan Museum of Art.

history people were able to sail across the open sea instead of just hugging the shore. The wood was in such demand that it was believed to have been used as far afield as Egypt to build Khufu's colossal funerary ships and Israel to build Solomon's Temple.

Another product that helped make Phoenicians the masters of the Mediterranean commercial trade was their near-monopoly on Tyrian purple, a spectacular red-purple dye from the secretions of predatory murex sea snails.[b]

The Phoenicians introduced viticulture and winemaking to areas in present-day Algeria, Egypt, France, Greece, Italy, Portugal, and Spain. In so doing, they also reportedly disseminated grape varieties that are still prized in Europe.[4] So valued was the Phoenician knowledge of wine that when the Romans sacked Carthage (originally a Phoenician colony located on the Mediterranean coast of modern-day Tunisia), the army reportedly was instructed to save the 28 books by Mago (unknown epoch), who had written classic works on agriculture, including some of the earliest texts on viticulture (the cultivation and harvesting of grapes) and viniculture (the cultivation and harvesting of wine grapes specifically).

Although the Phoenicians invented the precursor of the modern alphabet, little of their writing survives today. While the Mesopotamians inscribed records in cuneiform script on clay tablets, the Phoenicians, like the Egyptians, wrote on papyrus (derived from the Greek word *papuros*, meaning "paper"). In the dry, desert climate, inside Egyptian tombs, these papyri survived, but in the more humid coastal climes of the Levant (area including present-day Israel, Jordan, Lebanon, Syria, and southern Turkey) they did not. Even the works of Mago — which were rescued and brought to Rome, where they were translated into both Greek and Latin — have disappeared and are known only through citations by Roman writers.[c] Notably, no known documentation exists with respect to the Phoenicians' possible use of wine for medicinal purposes.

In the absence of written accounts, significant advances in underwater archaeology — particularly side-scanning sonar and deep-sea submersibles — are yielding abundant information about the wine culture of the Phoenicians and other citizens of the ancient Mediterranean. Previous finds were made by sponge divers and scuba divers who were working in depths of less than 100 feet. Over the past three decades, however, astonishing finds of Phoenician shipwrecks off the coasts of southeastern Spain, Israel, and Malta reveal details about international trade, shipbuilding techniques, and even wine composition.[14] These wrecks, some of which have been dated to ca. 750 BCE, typically contain numerous amphorae (the preferred shipping containers of the ancient Mediterranean; amphorae are also known as "Canaanite jars" because they were the Phoenicians' container of choice), and laboratory investigations have found that the wines therein were both resinated and filled with herbs, an indication that they were probably used for therapeutic purposes as well as enjoyment.[15]

Advances in human and plant genetics also are providing a better understanding of the Phoenicians and their wine. Scientists now believe that the Phoenicians were growing grapes that originated in the Caucasus, and that some of Europe's major grape varieties originated in Canaan.[4] Further progress in both underwater archaeology and genetics will continue to illuminate current understanding of ancient peoples and their wines.

[b] Recent archaeological research on Phoenician weapons determined that some of their steel spearpoints were stronger than any metal produced until the advent of the Bessemer steel process in 1856. Further research found that the key component in the steel's production was calcium produced by the crushing of the shells of these sea snails.[13]

[c] Mago's lost works are among the "Holy Grails" of classical philology.

Fit for a Pharaoh: Wine in Ancient Egypt

In Egypt, a taste for wine was inculcated thousands of years ago. Wine and wine making are depicted on obelisks, papyri, and sculptures and in vividly colored and highly evocative tomb paintings. One early oenophile (wine connoisseur) was King Scorpion I, whose tomb (ca. 3150 BCE) in Abydos contained 700 hundred jars of wine that are believed to have been imported from the eastern Mediterranean, including present-day Israel, Jordan, Lebanon, and Palestine. Laboratory analysis by McGovern and his team showed that Scorpion's wine contained not only terebinth resin but also coriander (*Coriandrum sativum*, Apiaceae), lemon balm (*Melissa officinalis*, Lamiaceae), mint (*Mentha* spp., Lamiaceae), sage (*Salvia officinalis*, Lamiaceae), savory (*Satureja* spp., Lamiaceae), senna (*Senna* spp., Fabaceae), and thyme (*Thymus* spp., Lamiaceae).[16] These herbs may have been added to improve flavor, slow spoilage, and enhance healing properties, since all are still used for both culinary and therapeutic purposes.

The Egyptians found that much of their territory was unsuitable for growing grapes, as was the case in Mesopotamia, but they determined that grape vines would flourish in the fertile soils of the Nile Delta, where viticulture was established around 3000 BCE. Again, similar to the situation in Mesopotamia, because production was limited, wine in Egypt remained primarily the drink of the pharaohs and other members of the ruling classes, while the masses drank beer.[2,10]

Grape *Vitis vinifera*
Photo ©2021 Steven Foster

As wine was the preferred beverage of the king, priests, and leading officials, winemaking became a celebrated activity in ancient Egypt, appearing in numerous tomb pictographs and paintings. Winemaking is illustrated vividly in pictographs within the tomb of Ptahhotep (late 25th century to early 24th century BCE), a vizier and philosopher, in Saqqara. Famous paintings of viticulture are found in Thebes in the tomb of Nakht (ca. 1400 BCE), an astronomer and priest who was laid to rest surrounded by strikingly colorful depictions of grape cultivation and harvesting.

Numerous medical papyri have survived — the Kahun (ca. 1900 BCE), the Edwin Smith (ca. 1650 BCE), the Ebers (ca. 1550 BCE), the Hearst (ca. 1500 BCE), the London (ca. 1350 BCE), and the Berlin, also known as the Brugsch (ca. 1350 BCE) — that provide detailed information on medicines used in pharaonic Egypt.[17] Wine features as an important component in many of these, such as this recipe from several medical records like the Ebers Papyrus: "To eradicate asthma: honey 1 [mouthful], beer 8 [mouthfuls], wine 5 [mouthfuls], are strained and taken in 1 day."[1]

The Egyptian wine-making process is depicted in a painting from the tomb of Khaemwaset, one of the sons of Ramesses II. 13th century BCE. Image courtesy of The Yorck Project.

Wine also appears in the Ebers Papyrus as a component in treatments for digestive problems and jaundice. It is prescribed in the Hearst Papyrus, the London Papyrus, and others to treat ailments as diverse as what appear to be epilepsy, fevers, and wounds. Wine was valued as a component in which medical plants and their compounds could be dissolved and consumed. Wine-based medicaments also were used in salves and enemas and applied to bandages.

In the London Papyrus, wine serves as a component in a treatment for aural discharge: "Medicament for an ear that is watery: Salt, heat with good wine; you apply it after cleaning [the ear] first. You scrape salt, heat with wine, and apply it for four days."[1]

Lucia (1963) also makes an important observation about these Egyptian prescriptions that feature wine and other plants and plant products like anise (*Pimpinella anisum*, Apiaceae), caraway (*Carum carvi*, Apiaceae), castor bean (*Ricinus communis*, Euphorbiaceae), coriander, cumin (*Cuminum cyminum*, Apiaceae), dill (*Anethum graveolens*, Apiaceae), frankincense (*Boswellia* spp., Burseraceae), myrrh (*Commiphora myrrha*, Burseraceae), and opium:

> The fact that Egyptian papyri written at dates several centuries apart are often found to contain identical prescriptions suggests that some of the remedies must have accomplished their purpose with regularity. This continuous recording of the therapeutic effects constitutes the beginning of [therapeutic] lore.[1]

Perhaps the most famous pharaoh of ancient Egypt also looms large in wine history. Tutankhamun (ruled ca. 1336-1327 BCE) was entombed with 36 amphorae of wine to accompany him to the afterlife. His funereal wine cellar included both red and white wine, and 26 of the jars are labeled with the name of the winemaker, the location of the vineyard, and the year of production — not unlike the wines of today, and proof that a royal winemaking industry was flourishing.[18]

Recent investigations of ancient Egyptian wine residues reveal that these ancient peoples added numerous spices and healing herbs. Healing plants apparently incorporated into some of these wines include coriander, lemon balm, mint, rosemary (*Salvia rosmarinus*, Lamiaceae), sage, savory, senna, and thyme.[16] Whether these species were added to slow spoilage, imbue a certain taste, or actually heal is impossible to discern at this point, although it seems highly likely that they were selected for at least one and possibly all of these purposes.

Not only was wine used because of its efficiency in extracting many of the pharmacologically active compounds of plants, it also often served to mask the bitterness of some of these herbs. Additionally, not all the unpleasant, purportedly therapeutic compounds added to wine were derived from plants (e.g., Egyptians treated epilepsy by adding ground donkey testicles to wine).

Wine in Religious Texts

The medical lore described in the Five Books of Moses, the Pentateuch (the first five books of the Hebrew Bible), draws heavily on Egyptian therapeutic traditions. As Moses was said to have been raised in the palace of the Pharaoh, he would have presumably learned much about Egyptian medicine.[d]

The Old Testament, believed to have been written before 400 BCE, repeatedly mentions medicinal uses of wine, including its mixture with olive (*Olea europaea*, Oleaceae) oil and balsam as a wound dressing. One of the sayings of Lemuel, a king mentioned in Proverbs 31, is to "give … wine unto those that be of heavy heart," implying that it serves as a mood enhancer, while another verse states, "Let him drink and forget his poverty, and remember his misery no more," suggesting its value as both a mood enhancer and a sedative. Psalm 104 states that "wine … maketh glad the heart of man" (Psalm 104:15).

In fact, grapes and wine are mentioned more often than any other plant in the Bible; so much that Hanneke Wilson states in *The Oxford Companion to Wine* (Oxford University Press, 1994) that "The Bible is not suitable reading for teetotalers."[19] In the Book of Genesis, Noah plants a vineyard as soon as the Great Flood subsides, and becomes the first person to produce wine, later becoming inebriated. Nonetheless, the implication was that viticulture represents progress in the development of civilization.

The Talmud states that wine is beneficial for treating problems of the heart, eyes, and bowels and possibly as a treatment for impotence.[1] In the text, a piece of bread soaked in wine is applied to infected eyes. The Talmud also claims that "wine taken in moderation induces appetite and is beneficial to health" and "wine is the foremost of all medicines; wherever wine is lacking, medicines become necessary."[20]

[d] Biblical scholars debate whether Moses was a historical figure, a composite of several individuals, or merely a myth. In any case, there were longstanding contacts between the Hebrews and Egyptians.

Wine has always served multiple purposes in Jewish religion and culture. Every major event, from birth to death, from weddings to holidays, involves the drinking of wine. In *The Story of Wine* (Mitchell Beazley Publishers, 1989), Hugh Johnson writes, "Jewish devotion to wine runs through their law and literature. It is the very essence of their civilization."[18] Wine, for example, is served at circumcision ceremonies and applied to the incision to prevent infection, and the newborn is sometimes orally dosed with a few drops as an analgesic.

Wine Culture in Ancient Greece

Wine also has been described as the touchstone of ancient Greek civilization, central to their cultural identity. Ancient Greeks believed that truly civilized people spoke Greek and drank wine. Ignorance of the Greek language and viticulture, especially by cultures that favored beer, was regarded as the hallmark of barbarians and savages.[e] As both a drink and a libation, wine served as a key component in Greek rituals and rites of passage including burials, marriages, sacrifice, and worship of the wine god Dionysus.[22]

Wine was enjoyed for its own sake but also served as a dietary, religious, and economic staple, and was a driving force in the colonization of much of the Mediterranean.[f] In a mountainous country with little arable land and no major rivers, the seafaring Greeks looked elsewhere to develop trade while expanding their wine culture further afield. In that sense, some might say that wine fueled a significant portion of the spread of Western civilization.

[e] The Greeks and Romans shared a disdain for both beer and beer drinkers. The Emperor Julian (331–363) composed a poem in which he claimed the scent of wine was of nectar, while the smell of beer was that of a goat.[21]

[f] By the eighth century BCE, the Greeks had colonized southern Italy and had imported and established their system of viticulture. They referred to the region as *Magna Graecia* ("Great/Greater Greece") as well as *Oenotria*, supposedly meaning "land of trained vines."[18] Whether this colonial expansion was driven by the search for new and better wine-friendly substrates — the rich volcanic soils of Italy are markedly better than those of Greece — the desire to expand their influence and trade routes, the human urge to explore the unfamiliar, or some combination of all of these is uncertain. One thing is clear: the drive to spread wine culture and the creation of international trade networks can be considered one of the wellsprings of capitalism.

Interior painting on a Greek wine cup showing the legend of Dionysus. ca. 550 BCE. Photo ©2021 Carole Raddato

A Timeline of WINE

Historical Highlights from the Ancient Mediterranean World

8000 BCE*	The oldest extant proof of wine production is pottery shards of vats that once held wine — dated to ca. 8000 BCE — which were excavated in what is now the Republic of Georgia.[2]
7000 BCE	The world's first wine culture is believed to have emerged in Transcaucasia — a region roughly comprising what today are the countries of Armenia, Azerbaijan, and Georgia and adjacent regions of both Iran and Turkey — by at least 7000 BCE.[2]
4000 BCE	Evidence of the most ancient winery known, believed to be in use as early as 4000 BCE, was found in the Areni-1 cave complex in central Armenia. Pottery shards, cups, fermentation vats, storage jars, and a wine press were uncovered at this site.
3150 BCE	The tomb of King Scorpion I (ca. 3150 BCE) in Abydos, Egypt, contained 700 hundred jars of wine believed to have been imported from the eastern Mediterranean. Scorpion's wine also contained terebinth resin and several herbs, which may have been added to improve flavor, slow spoilage, and/or enhance healing properties.[16]
3000 BCE	The Egyptians found that much of their territory was unsuitable for growing grapes, but they determined that grape vines would flourish in the fertile soils of the Nile Delta, where viticulture was established around 3000 BCE.
2600–2400 BCE	The first known depiction of wine drinking is featured on the "Standard of Ur" — a Sumerian box dated to 2600-2400 BCE. Now on display at the British Museum, the artwork portrays a king seated on a carved stool while being toasted by six attendees holding wine cups.
2200 BCE	A cuneiform tablet from the ancient city of Nippur in the Iraqi desert, dated to about 2200 BCE, features what is widely regarded as the world's oldest medical prescription.
1550 BCE	Wine features as an important component in recipes found in many ancient medical papyri, such as the Ebers Papyrus.
14th Century BCE	Tutankhamun (ruled ca. 1336-1327 BCE) was entombed with 36 amphorae of wine to accompany him to the afterlife. His funereal wine cellar included both red and white wine, and 26 of the jars are labeled with the name of the winemaker, the location of the vineyard, and the year of production.
750 BCE	The Phoenicians, the successors of the Canaanites, flourished from approximately 1200 to 539 BCE. A Phoenician shipwreck with a large cargo of wine, found by Robert Ballard, PhD, was dated to 750 BCE.[4]
700 BCE	Wine played a major role in ancient Greek life and was used casually, in rituals, and medicinally.
500–300 BCE	Xenophon (430–354 BCE) and Plato (428/7–348/7 BCE) believed that the moderate consumption of wine had health and wellness benefits.
First Century CE	Dioscorides recommended the use of wine for a wide range of illnesses, including cardiac ailments, digestive issues, and respiratory problems. Like Hippocrates, he specified which wine was to be taken for each malady, distinguishing carefully between the effects of old, new, dry, and sweet wines.
	Pliny the Elder (ca. 23/24–79 CE) was a strong proponent of the use of wine for therapeutic purposes. The 23rd volume of his 37-book encyclopedia *Naturalis Historia* is devoted to the medical uses of wine.
	Evidence suggests that wine grapes were cultivated throughout Pompeii (79 CE), including at least one sizeable vineyard with more than 2,000 grapevines on a plot of land previously believed to have been a cattle market.[26]
100–300 CE	Galen (129–ca. 216) became the last dominant figure in the Greco-Roman medical tradition known for employing wine as one of his most essential therapeutics. Galen was a major proponent of wine as medicine, particularly as an anti-infective wound dressing.
800–1100 CE	Muslim healers like Rhazes (Abū Bakr Muhammad ibn Zakariyyā al-Rāzī; 854–925) and Avicenna (Ibn Sina; 980–1037) employed wine primarily for external purposes such as wound dressings.

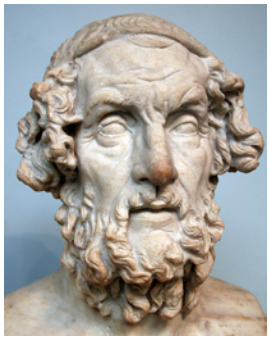
* All dates are approximate.

Photo ©2021 Matthew Magruder

Wine featured as the centerpiece of the famous symposium (derived from a Greek word meaning "drinking together"), one of the most vital social events in ancient Greece. A symposium was a lively wine-centered feast, at which a range of topics were debated and discussed (Standage described the process as rational inquiry through adversarial discussion), which helped lay the foundation for aspects of Western law, medicine, philosophy, and science. Both Plato (428/7–348/7 BCE) and Xenophon (ca. 430–354 BCE) recounted discussions at symposia they attended, and depictions of these drinking parties are common illustrations on Greek vases from the fifth century BCE.

An enduring aspect of ancient Greek culture is their system of medicine, which codified and systematized knowledge of health and healing. As was the case with the previous cultures discussed, wine played a prominent role.

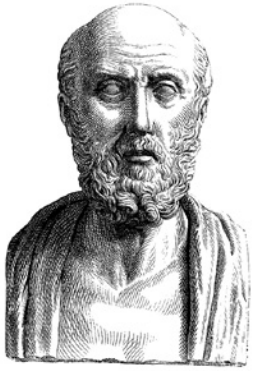
Homer



Though Hippocrates (ca. 460–370 BCE) is widely regarded as the "father of medicine," the first detailed accounts of ancient Greek medicine were sung by a blind poet: Homer. Almost 150 wounds are mentioned in the *Iliad* and the *Odyssey*, and considerable knowledge of medical practice is featured in both. Homer displays such detailed understanding and insight about wounds and treatments that some have suggested that he may also have been a physician. And wine is the medicine most frequently mentioned in both these epics. The Greek warriors returning home in the *Odyssey* carry wine, water, and grain with them. And the Trojans also drink wine, as does the Cyclops!

Hippocrates

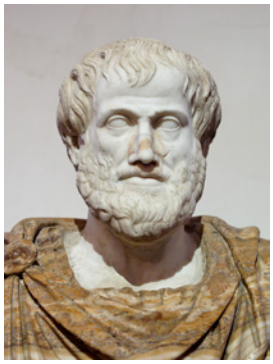
Born several hundred years after Homer during the epoch of Classical Greece, Hippocrates remains respected and revered more than 2,000 years later for launching the scientific study and treatment of disease. He is essentially the first major figure in the history of medicine to adopt an empiric approach, rather than attribute disease or healing solely to the spirit world.



One of the famous dictums attributed to Hippocrates was that "natural forces within us are the true healers of disease"; in other words, the human body is, to a large extent, self-regulating and self-healing, usually requiring only a bit of assistance in terms of exercise, fresh air, judicious use of medicine, and an optimal diet, of which Hippocrates considered wine an important component. He also recommended wine as preventative medicine and regarded regular consumption as a key to good health.

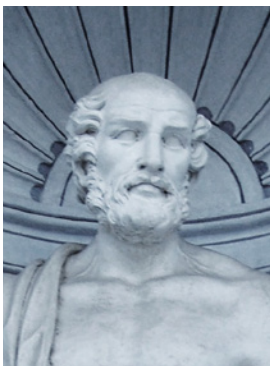
Hippocrates used wine as a diuretic and febrifuge (to reduce fever) and to treat many different ailments, including anxiety, eye pain, obstinate ulcers, and head wounds. In one famous passage attributed to him, he wrote, "No wounds should be moistened with anything except wine." Hippocrates was one of the first to write that different wines had different therapeutic properties (e.g., sweet white wines are diuretic, while tannin-rich red wines are antidiarrheic). According to Lucia, "[Hippocrates] made no extravagant claims for wine, but incorporated it into the regimen for almost all acute and chronic diseases, and especially during the period of convalescence."[1]

Aristotle



Hippocrates' fellow Greeks Aristotle (384-322 BCE), Plato, and Socrates (ca. 469-399 BCE) all commented on the value and uses of wine. Aristotle may have learned something about the medicinal value of wine from his father Nicomachus (unknown to ca. 374 BCE), who served as court physician to the King of Macedon, Amyntas III (unknown–370 BCE). In turn, Aristotle's most esteemed pupil was Alexander the Great (356–323 BCE), perhaps the greatest warrior of the ancient world. Generals are concerned for the welfare of their troops, if for no other reason than to be able to heal their wounds and send them back into battle. Undoubtedly, Aristotle, as the greatest polymath of his day, likely would have learned from his father of the medicinal value of wine and would have passed this wisdom on to his pupil Alexander.

Theophrastus



Theophrastus (371/0–287/6 BCE) was a pupil, colleague, and eventual successor of Aristotle. He often was deemed the "father of botany" because he wrote the first extensive treatise on plants covering plant structure, growth, and reproduction. Known in English as *Enquiry into Plants* (*Historia Plantarum*), it features detailed descriptions of many species, both native and foreign, with accounts of their uses. The book has had an effect on botany and medicine for more than 20 centuries. He further recorded the use of perfumed wines and their effect on the sense of taste. Theophrastus also made enduring contributions to viticulture: he wrote about the effects of terroir (environmental conditions that affect wine's flavor and aroma) and conditions for planting, as well as methods of grafting and pruning.

Wine in the Greco-Roman World

Greek civilization and wine culture massively impacted the Romans. Educated Romans spoke Greek as a second language and knew the *Iliad* and the *Odyssey* as some now know the Bible or the Quran. The Roman world drew heavily on Greek architecture, art, coinage, drama, literature, philosophy, religion, warfare, and, in particular, medicine and viticulture. The cultivation and consumption of grapes and wine tightly linked the cultures of Greece and Rome.

The questions of who the Romans were and whether they knew of cultivated wine grapes before the arrival of the Greeks on the Italian Peninsula are intricately intertwined. The Greeks had colonized southern Italy as early as the eighth century BCE. Recent genetic analyses have demonstrated that the inhabitants of the Roman world were a mixture of local Italian tribes — groups like the Etruscans, Oscans, and Samnites — as well as relative outsiders like the Anatolians, Greeks, and Persians. Per Brian Muraresku, a scholar on the ancient Mediterranean: "The original inhabitants of the Italian Peninsula were probably cultivating grapes and making wine in a relatively desultory fashion prior to the eighth century BCE, but it was in all likelihood the Greeks who introduced a culture of viticulture" (B. Muraresku, personal communication, August 7, 2020).

Stuart Fleming, the author of *Vinum: The Story of Roman Wine* (Art Flair, 2001), described the importance of wine to the ancient Romans:

> [It] was truly a central element of Roman everyday life. [Wine] was not just something which enhanced a meal or gave zest to a party. Rather, it was central to Roman overseas trade policies and political interactions with the peoples of their provinces; and it was an integral part of health care practices, of religious practices (initially pagan and cultic, but later on, Christian as well) both in life and in death. In Roman times wine was something with huge social overtones, in the sense that the quality of wine consumed was such an immediate reflection of status, senator to slave.… [T]hough some Roman vintners and traders did make a great deal of money out of wine production, profit was by no means their only motivation. Truth is, the Roman psyche was locked into Rome's origins among Italy's sturdy agricultural stock, so any kind of investment in farming, including viticulture, had a special meaning and a special virtue far beyond any we can instinctively imagine today.[23]

The Greek loss at the Battle of Corinth in 146 BCE marked the end of the Achaean Confederation and resulted in Roman rule of Greece. Despite Roman superiority on the battlefield, their healers were comparatively unsophisticated and unsuccessful, and thus some Greek physicians were brought to Rome where they began to practice their medicine. One of the first of these arrivals who helped establish Greek medicine as a respected discipline was Asclepiades (ca. 129/124–40 BCE; named after the Greek god of healing, Asclepius), who rose to such prominence that he served as physician to Cicero (106–43 BCE). His approach featured a healthy diet, exercise, music therapy, and cleanliness (he is said to have invented the shower). So frequently did Asclepiades prescribe wine to his patients that he earned the nickname *oinodotes* — "giver of wine."[24]

Dioscorides

Another towering figure in the history of medical wine and medicinal botany was Pedanius Dioscorides (first century CE), a Greco-Roman physician who traveled widely throughout the Empire. His book *De Materia Medica* created the template for the great majority of herbals that followed and served as the prototype for the modern pharmacopeia. Together with the works of Theophrastus and Pliny the Elder, *De Materia Medica* served as a principal authority on botany and, to some degree, medicine for more than 1,500 years. Written in Greek, it was translated into Latin, Arabic, and, in 1665, English. *De Materia Medica* was a major influence on botany and medicine in both the Christian and Islamic world and is considered history's most widely read botanical work. Dioscorides' enduring genius was turning medical botany into an applied science.

He recommended the use of wine for a wide range of illnesses, including cardiac ailments, disorders of the digestive system, and respiratory problems. Like Hippocrates, he specified which wine was to be taken for each malady, distinguishing carefully between the effects of old, new, dry, and sweet wines. Dioscorides also recommended therapeutic uses for other parts of the grape vine, including the flowers, leaves, stalks, and tendrils.

Pliny the Elder

A contemporary of Dioscorides, Pliny the Elder (ca. 23/24–79 CE) was both a scholar and an army and navy commander. Pliny attempted to combine all known knowledge into a 37-book encyclopedia — the *Naturalis Historia* — including everything from astronomy to zoology. Though he was for the most part more a compiler than a researcher, he claimed to have drawn information from more than 2,000 treatises written by nearly 500 Greek and Roman authors. Most of those original references have been lost, meaning that Pliny's encyclopedia contains a library of information that would otherwise have disappeared.

Roman fresco showing Bacchus and an agathodaemon serpent (a vineyard spirit) from the *Casa del Centenario* in Pompeii. Museo Archeologico Nazionale (Naples). Image courtesy of Wolfgang Rieger.

Pliny was a strong proponent of the use of wine for therapeutic purposes. The 14th book of his encyclopedia focuses almost exclusively on wine, and in contrast to most of his writings is believed to be based primarily on personal observations. Book 17 conveys considerable information on viticulture, while number 23 is devoted to the medical uses of wine. Pliny knew wine well: He mentioned 200 grape varieties, 50 types of Roman wines, 38 kinds of foreign wines, 18 varieties of sweet wines, and seven types of salted wines.

He ascribed special therapeutic capabilities to honeyed wines, salted wines, and wines into which medicinal herbs had been dissolved. For example, he recommended wine flavored with anise and bitter almonds (*Prunus* spp., Rosaceae) as a mouthwash; wine with rue (*Ruta graveolens*, Rutaceae) for stings of bees, hornets, and scorpions, and the bites of spiders and rabid dogs; wine with saffron (*Crocus sativus*, Iridaceae) as a diuretic and to relieve itching; and wine with "nep" (probably catnip, *Nepeta cataria*, Lamiaceae) to promote menstrual discharge and frighten away snakes. He wrote that "wines possess the remarkable property of drawing into themselves the flavor of other plants" and "there are two liquids especially agreeable to the human body: wine on the inside and olive oil on the outside."[9] Ever the investigator, he died in 79 CE when he sailed from Misenum (Miseno) to nearby Pompeii to more closely observe the eruption of Mount Vesuvius and rescue a family friend.[g,18]

Wine in Pompeii

Much of what is known about Roman wine culture has been learned through excavations of Pompeii and nearby sites such as Herculaneum, Oplontis, and Stabiae. The eruption of Mount Vesuvius simultaneously destroyed and preserved these towns. Roman devotion to wine is depicted in numerous paintings and mosaics of grapes, wine, vineyards, and the wine god, Bacchus. The ruins brim with the remains of vineyards, wine presses, wine vats (dolia), and wine jugs (amphorae).[h]

Pompeii served as an epicenter of trade in wine, shipped both to and from many corners of the Empire.[i] The town and its environs served as Rome's principal source of wine, due in no small part to the rich and productive volcanic soil. So passionately devoted were the Pompeiians to their favorite beverage that many of the houses were decorated with figures of Bacchus. One particularly poignant painting in the House of the Centenary features Bacchus dressed in grapes, standing next to Vesuvius, whose slopes are covered in grapevines.

Much of what is known about how and where grapes were planted in ancient Pompeii is due to the ethnobotanical detective work of Wilhelmina Feemster Jashemski (1910–2007). She removed the volcanic debris that filled cavities created when roots decayed and filled them with plaster. She was then able to determine precisely which crops had been planted and where. Her research proved that grapes were cultivated throughout Pompeii, including at least one sizeable vineyard with more than 2,000 grapevine root cavities within the confines of the city itself, on a plot of land previously believed to have been a cattle market.[26]

At the conclusion of *Gardens of Pompeii* (Oxford University Press, 2000), Annamaria Ciarallo writes:

> [In Pompeii,] the great importance of viticulture and wine production was not due solely to the popularity of wine that was consumed for pleasure. It was an extremely important basic constituent of the so-called medicated wines, which had been steeped with plant essences containing active ingredients. Medicated wines were kept in the home pharmacy as medicines to treat short-lived ailments, such as stomach ache, cough or insomnia. This practice demonstrates how one could arrive in an intuitive manner at knowledge of the extractive capacity of alcohol, even though its nature obviously remained unknown.[27]

Though investigations at Pompeii have not yet yielded information on the use of wine for medical purposes, one ancient library, with papyri still relatively intact, is still being investigated, and a quarter of the ancient city remains unexcavated.

Galen

Approximately a century after Pliny died at Pompeii in 79, Galen (129–ca. 216) became the last dominant figure in the Greco-Roman medical tradition known for employing wine as one of his most essential therapeutics. In *History of Pharmacy* (J.B. Lippincott & Co., 1949), Kremers and Urdang wrote:

> Galen was the first physician if not the first scientist to explain that observation and experiment are the principal sources of knowledge and to act accordingly…. With Galen, the Greco-Roman epoch of medicine and pharmacy reached its climax. For a long time, it was essentially his treatises and the materia medica of Dioscorides which in innumerable copies, commentaries and extracts … disseminated medical and pharmaceutical wisdom throughout the western world.[28]

[g] Scientists conducting recent genetic analyses of bones recovered from Pompeii claim to have identified what they believe to be Pliny's skull.[25]

[h] The scale of the wine exported from Pompeii beggars belief. The wreck of a single ship that had sailed from the Pompeii region and then sunk off the coast of northwest Italy contained more than 10,000 amphorae — the equivalent of 33,000 modern wine bottles.

[i] Italian viticulturists — after studying archeological remains of seeds and wine residues and even frescos depicting grapevine cultivation — believe they have been able to recreate some of Pompeii's ancient wines. Nonetheless, the global wine industry is devolving toward monoculture: of the more than 1,368 known wine grape varieties, 80% of the world's wine is made from only 20 varieties of grapes.[19]

Fresco depicting the "god-like" properties of wine from the *Sala di Grande Dipinto* in the Villa dei Misteri near Pompeii. Image courtesy of Wolfgang Rieger.

So widely renowned was Galen that he served as personal physician to several Roman emperors, including Marcus Aurelius (121–180). But the most formative experience of his career was when he served three years as surgeon to the gladiators in his native Pergamon (on the western coast of present-day Turkey). His observations and treatments of injured fighters provided unparalleled insight into the human body and the form and functions of organs. He referred to the terrible gladiatorial wounds he treated as "windows into the body."[29]

Galen was a major proponent of wine as medicine, particularly as an anti-infective wound dressing. He used wine to clean out fistulous abscesses. In cases in which gladiators had been eviscerated, he soaked the exposed organs in wine before stuffing them back into the abdominal cavity and then sewing up the wound.[1,11]

Galen's legacy was profound: a system of diagnosis and treatment that dominated Western medicine for well over a thousand years. Some of his therapeutic formulations of natural products, many of which contained wine, were known as Galenicals. Today, the term more commonly refers to preparations consisting of one or several natural ingredients but still pays homage to this medical pioneer.

Importance of Wine in Christianity and Islam

As the Christian world began to develop, wine maintained an important role, especially as a symbol. Jesus called himself "the true vine," (John 15:1) and his first miracle was turning water into wine. No other plant besides the wine grape is more intimately associated with his life and ministry.[5] At the Last Supper, Jesus declines the wine on offer, preferring to wait until he can consume it in the Kingdom of his Father (Luke 22:18).[j]

The early accounts of Christianity such as the New Testament feature many mentions of wine but markedly fewer references to therapeutic uses than the Hebrew texts that precede them. One famous exception is the Parable of the Good Samaritan in the Gospel of St. Luke, in which the

[j] Recent research featured in the book *The Immortality Key* (St. Martin's Press, 2020) notes the presence of the remains of psychotropic plants like opium, cannabis (*Cannabis* spp., Cannabaceae), and henbane (*Hyoscyamus niger*, Solanaceae) in ancient wine vessels discovered at the Villa Vesuvio near Pompeii at the exact time (79 CE) when Magna Graecia was Christianizing.[30] Some experts believe that these entheogens (substances that produce an unordinary state of consciousness) may serve as one possible explanation for at least a few of the early Christian miracles, and might link some of these foundational revelations — and wine — to the famous Dionysian Mysteries of ancient Greece (rituals in which intoxicants were used), which are vividly portrayed and remarkably preserved in frescoes at the Villa of the Mysteries in Pompeii.

Samaritan rescues a traveler beaten by robbers and applies olive oil and wine to his wounds. According to physician and wine historian Philip Norrie, St. Luke was originally a Greek physician and would therefore have known of the efficacy of wine as an antiseptic from the teachings of Hippocrates, and possibly Pliny and Dioscorides.[31]

Writers as diverse as Herodotus and Omar Khayyam (1048–1131) documented the Persians' devotion to wine. Hafez (1315–1390) — one of the most beloved of the mystic Persian poets, who was born and died in the city of Shiraz, formerly known as Persia's city of wine — composed poetry on the joys of love and wine. The Greek soldier-philosopher Xenophon, who fought both for and against the Persians, noted that they were well-aware of the antiseptic value of wine. Northwest Iran extends into the Caucasus region where winemaking originated. Zoroastrianism, the original major religion of Persia, starting around 500 BCE or earlier, was not opposed to wine.[4]

With the rise of Islam and its spread into Persia, the prohibition of alcohol led to many changes in this part of the cradle of viticulture and brought challenges for Persian and Arabic physicians. The Quran seemingly prohibits alcohol and therefore presented Arab physicians with a dilemma.

Much of Islamic medicine was influenced by Greek and Roman texts written by healers like Galen who championed the therapeutic value of wine. Muslim healers like Rhazes (Abū Bakr Muhammad ibn Zakariyyā al-Rāzī; 854–925) and Avicenna (Ibn Sina; 980–1037) used wine primarily for external purposes such as wound dressings. The first distillation of wine is believed to have been conducted by the Muslims (possibly by Rhazes); the process markedly increases the alcohol content and made possible the invention of hard liquor — an unintended irony.

Conclusion

More than any other plant or plant product, wine was regarded almost as a panacea in the ancient Mediterranean world. It was used as an analgesic, antibiotic, antidiarrheal, aphrodisiac, diuretic, menstruum, and soporific. Wine also was used to treat anxiety, asthma, cardiac problems, digestive problems, epilepsy, insect stings and spider bites, jaundice, respiratory problems, and wounds and to purify water. Several of these uses appear repeatedly in the historical record, undoubtedly due to the fact that wine is highly effective in some instances as an antimicrobial, painkiller, water sanitizer, and wound disinfectant.

Today, we know that wine, when included as a moderate addition to the diet, can reduce the risk of cardiovascular disease and may help ward off certain cancers as well. Research on wine's health benefits continues, including analyses of single components like resveratrol and its holistic benefits as part of the Mediterranean diet.[32]

It likely has been more than 10,000 years since the world's first wine culture emerged, but the appeal of this ancient beverage has endured. Socrates, quoted by Xenophon, observed: "Wine does in fact moisten the soul and lulls our pains to sleep … it revives our joys, just as oil does a flame."[33] HG

Dedication

I would like to dedicate this paper to four great teachers: the late Aritana Yawalapiti of the Xingu Indigenous Reserve (Brazil); Patrick McGovern, PhD, of the University of Pennsylvania; John Riddle, PhD, of North Carolina State University; and the late José de los Santos Sauna Limaco of the Sierra Nevada (Colombia).

Acknowledgements

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Mark Plotkin, PhD, LHD, *is an ethnobotanist who serves as the president of the Amazon Conservation Team (www.amazonteam.org). His most recent book is* The Amazon: What Everyone Needs to Know, *published by Oxford University Press (2020). He is a longtime member of the ABC Advisory Board.*

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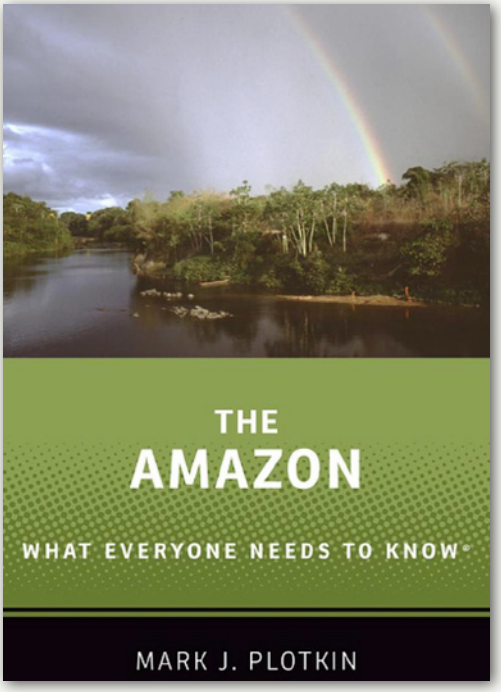
Grape *Vitis vinifera*
Photo ©2021 Steven Foster

The Amazon: What Everyone Needs to Know by Mark J. Plotkin. Oxford, UK: Oxford University Press; 2020. Softcover, 256 pages. ISBN: 978-0190668280. $16.95.

By Roger Mustalish, PhD

Mark J. Plotkin's, PhD, new book *The Amazon: What Everyone Needs to Know* begins with this brief excerpt from a 1799 letter by German explorer Alexander von Humboldt (1769-1859) describing his first journey into the Amazon rainforest with his colleague Aimé Bonpland (1773-1858), a French explorer and botanist: "Bonpland keeps telling me he will go mad if the wonders do not cease."



Plotkin then guides readers on their own journey into Amazonia, and the wonders do not cease. I have been fortunate to visit Amazonia nearly 100 times, and reading Plotkin's accounts of the magnificence of this world floods me with memories and continues to provoke thought and questions about its future. It is this approach — asking questions — that forms the framework of the book.

The book is structured into six broad thematic areas, including Geology, Soils, and Vegetation; Rivers; Amazonian Biota; Indigenous Peoples; History; and Amazonia's Uncertain Future. Within these categories, Plotkin poses 67 questions and then addresses them. The table of contents presents the questions and directs readers to the appropriate pages, which makes it easy to navigate the book. Questions include: What is the geological history of the Amazon? Why are bromeliads known as the aerial aquaria of the Amazon? What are Amazonia's most formidable predators? When did the first humans arrive in Amazonia? What is the impact of overhunting and overfishing in Amazonia? And most importantly: How can Amazonia be saved?

Most of these questions and answers permit Plotkin to step the reader through the immensity of Amazonia, and the superlatives do not stop. He notes that the flow volume of the Amazon River is more than the next eight largest river systems combined. In discussing the extensive terrestrial and aquatic biodiversity found in the forest, he mentions, for example, Peru's Manú National Park, which has more bird species than the entire United States and more butterfly species than all of Europe. On and on, the author describes the amazing Amazonia with passion and skill.

Plotkin has a gift for taking complex scientific, anthropological, socio-economic, and political concepts and translating them into a direct, clear explanation that invites the reader to join in the wonder of the region while also reflecting on how to address its tenuous future. It must be said, though, that at times Plotkin asks some unusual questions: Do vampire bats drink human blood? Is the tiny candiru catfish as terrifying as its reputation?

The 67 questions are skillfully arrayed throughout the book. Indeed, I found picking and choosing questions of interest and then going to that portion of the book was a wonderful way to explore Amazonia, and, at least for me, was more enjoyable than reading it from beginning to end. In addition, starting on page 201, notes for each chapter allow readers to delve more deeply into different subjects.

One can think of the broad themes of the book as scenes on a vast tapestry and the responses to the 67 questions as the threads used by Plotkin to weave the marvelous story of Amazonia. Readers can gaze at one part of the tapestry and later explore another portion, each time coming away with a better understanding of the nature of this extraordinary ecosystem.

For most of the narrative, Plotkin responds to the questions in a third-person voice, blending facts with his gift of storytelling. This certainly works well. Occasionally, though, he reverts to a first-person voice. That is when the book really comes alive. It takes on the feel of a conversation or a question-and-answer session between Plotkin and the readers. These portions are more reminiscent of the style of his book *Tales of a Shaman's Apprentice* (Viking, 1993).

While the book does indeed serve as a current guide to Amazonia, especially as it relates to current threats and efforts to protect the ecosystem, it is not a field guide per se, with comprehensive lists and descriptions of the flora and fauna. Nor is it a primer for students or the public in the style of John Kricher's *The New Neotropical Companion* (Princeton University Press, 2017), and it does not pretend to be. Rather, Plotkin vividly informs readers across an array of themes to explain the interconnectedness of this ecosystem, its importance, and the stake we all have in its protection.

Reading the book, a recurring question came to me: Given the many questions that could have been asked and answered, how did Plotkin arrive at the specific 67 in the book? It would be fascinating to know the

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decision-making process that led to these 67 questions being selected. That said, after reading and reflecting, a few questions of my own arose: What is happening to empower girls and women in Amazonia? Where will the next generation of conservation leaders come from? What skills will they need? What is the current status of primates? Are more botanical medicines and supplements awaiting discovery and commercial development? Would internet connectivity in remote Amazonian villages be a benefit or curse to residents? I have no doubt that readers of this book will have their own questions. Does this portend a Volume 2? One would hope!

In the conclusion of the book, Plotkin saves the most important question for last: How can Amazonia be saved? His careful analysis is both sobering and hopeful and can be summed up in these powerful thoughts:

> If the driving force behind all decisions that affect the great rainforest [is] merely maximizing short-term economic return to global elites, [then] the Amazon is doomed…. However, if we can modify our goals and our approach to encourage sustainable harvest and production and long-term planning while incorporating societal well-being … then there is most definitely hope.

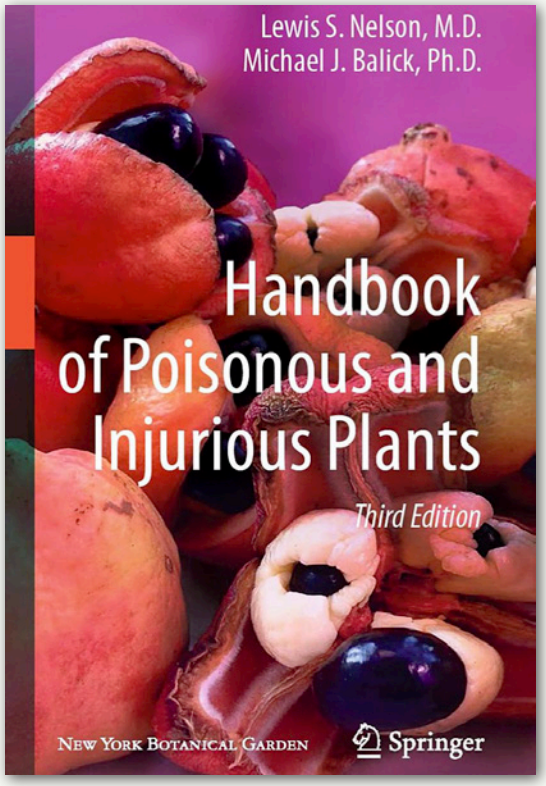
This book will inspire readers to embrace and empower that hope.

***Roger Mustalish, PhD**, is a professor emeritus at West Chester University of Pennsylvania and adjunct professor of environmental health at Creighton University in Omaha, Nebraska. He is the immediate past president and current vice president of the Amazon Center for Environmental Education and Research (ACEER).*

***Handbook of Poisonous and Injurious Plants**, 3rd ed.*, by Lewis S. Nelson and Michael J. Balick. New York, NY: New York Botanical Garden and Springer; 2020. Hardcover, 336 pages. ISBN-978-1-4939-8924-9. $59.99.

By Marilyn Barrett, PhD

I firmly believe that a collaboration across disciplines can produce a richness not obtained from authors of one discipline. The third edition of *Handbook of Poisonous and Injurious Plants* exemplifies this. It is a collaboration between Lewis Nelson, MD, an academic emergency physician with a background in toxicology, and Michael Balick, PhD, a botanist with expertise in ethnobotany and toxic plants. This book combines Nelson's experience in the clinical management of potential poisonings with Balick's solid foundation of botanical knowledge to discuss and identify the plants.



The first edition of this book was published in 1985 by the American Medical Association and written by Kenneth F. Lampe, PhD, and Mary Ann McCann. The second edition was published as a partnership between Springer and the New York Botanical Garden, where Balick is the research and training director and philecology curator at the Institute of Economic Botany. This arrangement was continued with this third edition. The first edition included information on poisonous fungi. According to the authors, this information was dropped for the second and third editions, as that is covered more adequately in other texts.

Handbook of Poisonous and Injurious Plants is an excellent reference book for clinicians, botanists, and anyone with an interest in plants. The book begins with background on botanical nomenclature and terminology. The botanical terms are accompanied by illustrations that help immensely with interpreting the definitions. The botanical section is extremely important, as the first step of working with plants is to identify them by their Latin binomial.

The book proceeds with a section on the clinical symptoms and management of poisonings. Plants are grouped into categories according to the mechanism of poisoning and/or chemical constituents known to have harmful effects: anticholinergics, calcium oxalate crystals, cardioactive glycosides, convulsants, cyanogenic compounds, gastrointestinal toxins, mitotic inhibitors, nicotine-like alkaloids, pyrrolizidine alkaloids, sodium channel activators, and toxic albumins. There are also expanded sections on plant-induced dermatitis and gastrointestinal decontamination.

The book includes tables with lists of plants associated with

dermatological irritations that would be useful for looking for a potential causative agent. One comment that struck me in particular was that children tend to ingest poisonous plants accidentally, whereas it is often intentional with adults — either for therapeutic, injurious, or psychoactive purposes. Another table I found particularly interesting was a listing of the top 10 plant exposures reported by US poison control centers in 2018. At the top was *Capsicum* (Solanaceae) species (chili peppers).

The bulk of the book is devoted to a catalog of individual plants arranged according to genus. Each listing includes Latin binomials, common names, botanical descriptions, geographical distributions, the toxic plant parts, and the chemical toxins, along with the clinical symptoms and suggested management of those symptoms. Each plant is beautifully illustrated with photographs, many of them provided by noted botanist, author, and photographer Steven Foster. Finally, each plant section is accompanied by references, which allow for further investigation.

I suggest updating the plant family names to those currently recognized by taxonomists. While the old family names, such as Compositae and Leguminosae, are comforting and familiar, using the more recent names, such as Asteraceae and Fabaceae, respectively, would make the plant listings current. In future revisions, a reference to the American Herbal Products Association's lists of standardized common names for plants in commerce in the United States might be useful for investigating adverse effects from dietary supplements. Another suggestion for future revisions, which I acknowledge might be challenging, would be to include more information about dosages. The authors note that "the dose makes the poison" and that most plant exposures do not result in toxicities. This makes it difficult for professionals and consumers to put plant exposures into context. These suggestions are minor and do not detract in any way from the value of the book.

I highly recommend this beautiful and well-laid-out reference book to anyone with an interest in potentially poisonous or injurious plants. HG

***Marilyn Barrett, PhD**, is a consulting pharmacognosist and a long-time member of the ABC Advisory Board.*

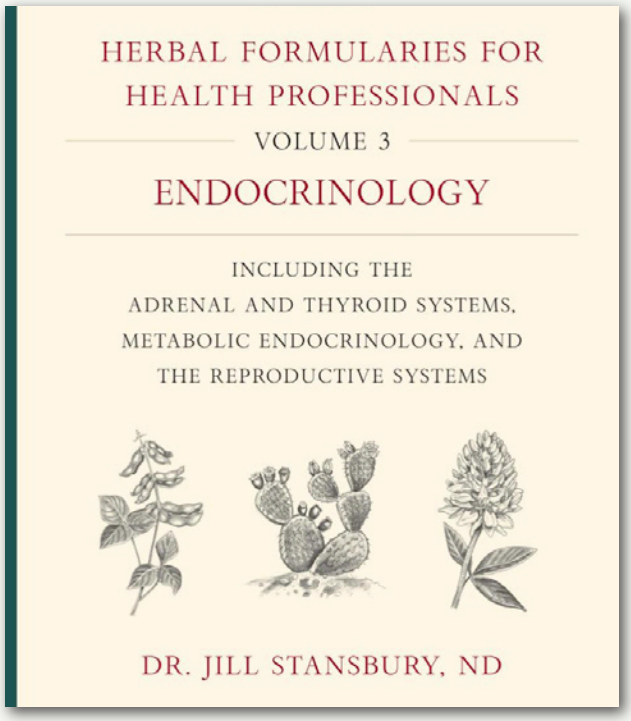
Herbal Formularies for Health Professionals, Volume 3: Endocrinology by Jill Stansbury. White River Junction, VT: Chelsea Green Publishing; 2019. ISBN: 9781603588553. Softcover, 272 pages. $49.95.

By Eric Yarnell, ND, RH(AHG)

This five-volume series on herbal formulations for professionals by Jill Stansbury, ND, is much needed. The lack of published works on this fundamental practice of natural medicine — formulating herbs into synergistic blends — has been a constant source of annoyance to me. Stansbury has taken on the difficult task of writing about formulating in all areas, and she is to be congratulated for her Herculean effort.

I recommend this volume as a good introductory work on herbal formulation for people with endocrine and reproductive problems. The author clearly had to walk a tightrope between presenting information for people new to formulating (whether students or conventional health care providers who never learned herbal medicine) and those who already have a fair bit of knowledge. Some sidebars in the book are useful for creating individualized formulas, such as "Fine Tuning Menopausal Transition Formulas" on page 138. Overall, I feel confident having my beginning botanical medicine students at Bastyr University, Southwest College of Naturopathic Medicine, and National University of Health Sciences look at many of her base formulas as a starting point in formulation for individual cases.

I do have several concerns about this volume that unfortunately lessen its utility. First, there is a lack of recognition of other widely used ways to formulate. Stansbury's simple



formulas, most with five herbs or fewer and in equal parts, do not reflect more sophisticated systems such as Chinese or Ayurvedic formulation, let alone more complex Western herbal formulation. This is appropriate in a textbook for beginners, which I contend this book is, but will leave intermediate prescribers wanting. An area of weakness in this regard are her various formulas for cancers, which I believe overlook the full potential of herbal medicine.

Second, there is a problematic lack of consistency. Sometimes, conflicting information is presented in the *materia medica*, such as on page 21, where yarrow (*Achillea millefolium*, Asteraceae) is listed as both warming and cooling, and this confusion is not addressed in the description of the herb. Some recipes state to use equal parts in unspecified amounts, but others give specific (equal) amounts. In some formulas, she lists the herbs followed by the amounts and in others this is reversed with no obvious reason as to why.

Third, the process of determining how much medicine to supply to a patient is a crucial oversight. Many of her formulas, at the doses stated, will last only a brief time, which is difficult to justify when treating patients with chronic conditions. For example, her Tincture for Uterine Fibroids on page 151 calls for dispensing 32 mL of the formula (also odd, as this would overflow a standard 1-oz or 30-mL bottle) at a dose of 0.5–1 teaspoon three to four times daily. At the lowest end of this dose, 32 mL would only last for four days! Is the patient to then get a larger amount after taking this tiny amount to ensure tolerability, or get refills every four days (presumably not, given the incredible inconvenience)? No explanation is provided.

Fourth, though Stansbury rightly points out that traditional knowledge is the basis of much of herbal medicine, her failure to cite any of the herbal references to which she refers throughout the book is upsetting. Including a general bibliography of at least the major references she employed while writing this text would show respect to those who came before her. It would also allow the reader to verify if the sources are being cited correctly. Or, if she intended to say that the oral traditions of world herbal knowledge were a major base of her writings, then she should cite those people from whom she obtained this knowledge, including their permission to use it here.

Fifth, though she criticizes the current emphasis on isolated, "active" constituents and describes the problems with research on them, she focuses a good deal on these constituents and recommends isolated constituents as therapies surprisingly often. For some herbs, such as sweet wormwood (*Artemisia annua*, Asteraceae) or Oregon grape (*Berberis aquifolium*, Berberidaceae), which have a rich literature on the synergy among their constituents, she presents only the constituents artemisinin and berberine, respectively, in her *materia medica* discussions. Both isolated constituents are recommended as treatments either alone or with only one other ingredient, which seems to have nothing to do with herbal or traditional medicine. I advocate dropping these and other single constituents she recommends from consideration in the book, as such information is readily available in numerous other books and on the internet. She should focus solely on formulating with whole herbs and extracts, or, if she is going to recommend isolated constituents, at least reinforce the need to combine them with the whole plant for synergy.

Unfortunately, Stansbury squandered the opportunity to use the *materia medica* descriptions to highlight and clarify the actions of the herbs. Each herb should have its energetics listed (at least whether they are cooling or warming). She refers to these properties frequently in the book but does not mention them in many herb descriptions. A simple list of major and minor actions also would be helpful. The short narratives she provides are not easy to find for quick reference and not complete enough for serious study. They put too much emphasis on preclinical research on isolated constituents and on use of herbs for specific diseases, which is odd given her stated philosophy that these are not a good basis for formulation.

Jill Stansbury's volume three is an acceptable text for use in a beginning herbal formulation class, but an experienced teacher will be needed to help guide students in using this tool. I would not recommend it as a stand-alone text or reference, but only in this particular teaching context. HG

***Eric Yarnell, ND, RH(AHG)**, is an assistant clinical researcher and adjunct faculty member in the department of botanical medicine at Bastyr University. He is president of Heron Botanicals and CEO of Red Root Pharmaceuticals.*

Walter H. Lewis 1930 – 2020

By Edward J. Kennelly, PhD

Walter H. Lewis, PhD, a renowned botanist whose expertise spanned the flora of multiple continents and disciplines as disparate as cytology and pharmacognosy, passed away peacefully in his home in St. Louis, Missouri, on November 17, 2020. He was 90 years old.

He is most widely known for the 1977 seminal book *Medical Botany: Plants Affecting Man's Health* (Wiley), cowritten with his wife and collaborator of 63 years, Memory Elvin-Lewis, PhD. At the time of publication, few books on this topic were as approachable to the public. Its publication coincided with growing consumer interest in herbal medicine and the herbal supplement industry in the United States, and it quickly became a standard reference for learning about the science behind medicinal plants. In his 1979 review for the *Journal of Natural Products*, Paul Schiff, Jr., PhD, noted: "A virtual plethora of subjects is discussed…. [T]he authors have assembled a large number of references on widely diverse subjects and presented a great deal of interesting material in an easily readable fashion."[1] The first edition sold more than 20,000 copies and in 2003 was extensively revised and republished under the title *Medical Botany: Plants Affecting Human Health.*

"Walter was a mentor, colleague, and friend," wrote American Botanical Council (ABC) Founder and Executive Director Mark Blumenthal (email, January 7, 2021). "He was a consummate gentleman, always very pleasant and courteous. He was one of the first academic experts on medicinal plants I ever met, and I first encountered him at the first Herb Trade Association Herb Symposium in 1977. In the late 1970s and early 1980s, the first edition of *Medical Botany* was one of my most-used references, and I was honored when Walter invited me to write a blurb for the 2003 revision. Over the years, Walter was always available, cooperative, and responsive to requests for [his] expert assistance. His death is a huge loss to the botanical medicine academic community in the United States and worldwide."

As a professor of biology at Washington University in St. Louis from 1964 to 2000, he taught a popular undergraduate course based on his book and not only instilled in his students knowledge of useful plants, but also engrossed them with tales of his adventures collecting medicinal plants from around the world. His last medical botany class at Washington University is vividly remembered by students who witnessed him arrive dramatically dressed in the style of the Jivaroan people from the Amazon basin, toting a dart gun; whether curare poison was painted on the dart tip is subject to debate.

Lewis' last doctoral student, Steven Casper, PhD, now a scientist at the US Food and Drug Administration, recalled (email, December 10, 2020): "His medical botany class was extremely popular, and the students were fascinated by the course and Dr. Lewis' amazing stories of his travels and research. He was always willing to talk with, help, and guide students. He was one of the rare gentlemen scholars and is greatly missed."

Joseph Jez, PhD, chair of biology at Washington University, wrote (email, December 11, 2020): "Walter was a great example of a scientist who truly explored, following the data and ideas from the bench into the rainforest. He will be missed by all."

Lewis was born on June 26, 1930, in Ottawa, Ontario, and first became interested in plants as a child in Victoria, British Columbia, where he was fond of growing plants. For his 12th birthday he asked for and received a greenhouse, learned to grow roses from his uncle, and started a small business selling them locally. Although his parents encouraged him to pursue dentistry (interestingly, his wife is a dental microbiologist and ethnobotanist), his passion for botany would be a guiding force throughout his life. After completing his undergraduate degree in biology at the University of British Columbia, he immediately began his doctoral work in plant biology at the University of Virginia as a DuPont fellow. Under the mentorship of Walter Flory, PhD, Lewis revised the genus *Rosa* (Rosaceae), and this thesis was recognized as one of the best in the state by receiving the J. Shelton Horsley Research Award from the Virginia Academy of Science in 1957.

Lewis published more than 300 papers about plants, which ranged from classical taxonomy, cytology, ethnobotany, phytochemistry, and ecology. Sir Ghillean Prance, DPhil, former director of the Royal Botanic Gardens, Kew, wrote (email to M. Elvin-Lewis, January 12, 2021): "I am really impressed with Walter's publication record and am glad to have this bibliography about so many different topics. … Walter will be missed by many people and has made a highly significant contribution to botany."

Late in his career, Lewis returned to his original interest in the genus *Rosa*. He helped revise the section *Rosa* in the *Flora of North America*, and the ninth volume of this flora (Oxford University Press, 2014) is dedicated to him. In 2013, he was named Rosarian of the Year by an affiliate of the American Rose Society. He also maintained a unique collection of native American roses at his large home garden in St. Louis. In one of his final rose publications in 2016, he described a new species, *Rosa memoryae*, which is native to Texas and named in honor of his beloved wife.[2]

Lewis' field work in botany took him to many near and faraway lands including Africa, North and South America, and Asia. In his role as the director of the herbarium at the Missouri Botanical Garden, he was the editor of the *Flora of Panama* (1965-1970). His work on American ginseng (*Panax quinquefolius*, Araliaceae) conservation led him to be among the first American scientists to travel to mainland China in the 1970s, where he participated in the First National Wu-Cha (*Acanthopanax*)* Symposium in Harbin, China, in 1978. This groundbreaking international interaction, only six years after US President Richard Nixon's historic trip in 1972, was covered by NBC News. At the symposium, Lewis presented a talk about his work on wild and cultivated populations of American ginseng.[3]

Lewis' work with his wife in West Africa in the mid-1970s laid the groundwork for their long-standing collaboration in the field of ethnobotany. As an ethnobotanist, Lewis was most well-known for his work among the native peoples of Peru. For more than 20 years, he and Elvin-Lewis worked as a team conducting research on the plants used by the Achual and other native peoples of that area. He was awarded a highly competitive grant from the International Cooperative Biodiversity Groups (ICBG) Program of the National Institutes of Health to study ethnobotany in the Andean tropical rainforests of Peru.

Gordon Cragg, PhD, who headed this program at the National Cancer Institute, noted that Lewis' legacy lives on through his ICBG-sponsored work (email, December 8, 2020): "Almost 4,000 plant species were collected, including a large number prescreened for human use by the Aguaruna themselves, and it is significant that these provided higher frequencies of bioactive secondary metabolites than those found in the flora as a whole. Since the cessation of Walter's ICBG grant support in the early 2000s, this invaluable plant collection has continued to be studied by most of the original team members and has been a source of a range of potential new anticancer, anti-infective, and wound-healing agents."

Michael J. Balick, PhD, vice president for botanical science and director and philecology curator of the Institute of Economic Botany at the New York Botanical Garden and ABC Board of Trustees member, wrote (email to S. Casper, December 11, 2020): "As a graduate student attending one of my first meetings of the Society for Economic Botany, I was understandably intimidated by all of the luminaries present in the group. I remember Walter Lewis, who was a friend of my advisor Richard Evans Schultes, coming over and introducing himself, inquiring about my work and telling me about his latest tropical expedition. That was emblematic of Walter: to care about the next generation of ethnobotanists and be helpful to all."

I was a doctoral student at Washington University in St. Louis and was mentored by both Lewis and Elvin-Lewis in my research on medicinal plants. Lewis was a gentleman and a scholar in the very essence of that phrase. His passion for botany was evident from the first time I met him. I conducted field work with him in Amazonia and learned not only about botany and science, but also how to work effectively with people from different backgrounds. In 2019, I traveled with Lewis, his wife, and Steven Casper to Ontario to be part of Elvin-Lewis' tribute as an outstanding Canadian scientist. While his mind was obviously impacted by Alzheimer's disease, he enjoyed engaging with people and was as polite and kind as I always remember him. He also remained passionate about plants, examining the local flora as we walked the streets of Guelph together.

Walter Lewis is survived by his wife, Memory Elvin-Lewis; his two children, Walter Jr. (Joanna Watt) and Memoria (Trevor Morse); and three grandchildren, Florence, Lilian, and Leander. The family is planning a home memorial service in June 2021 when the wild rose collection in his garden will be in full bloom. HG

***Edward Kennelly, PhD**, is a professor of biological sciences at Lehman College, City University of New York. He received his PhD in biology from Washington University in St. Louis in 1993 under the mentorship of Walter Lewis and Memory Elvin-Lewis.*

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* *Acanthopanax* is an older term for the genus currently known as *Eleutherococcus*.

William J. Keller
1942 – 2020

By A. Douglas Kinghorn, PhD, DSc

It is with profound sadness that I report that William "Bill" J. Keller, PhD, died at age 77 on October 29, 2020. Among his many contributions to the field of pharmacognosy, Keller was the long-term secretary of the American Society of Pharmacognosy (ASP) for about 30 years and an honorary member of ASP. He died due to complications from a serious fall in late 2019.

Keller began his duties as ASP secretary in 1985 and conducted these with great efficiency and reliability. In addition to being a bastion of ASP for so long, and someone who was approachable to young and older colleagues alike, he was also an excellent natural products scientist, who had a highly successful career in both academia and the dietary supplements industry.

Keller was born in Ware, Massachusetts, on November 13, 1942. He received his BS in pharmacy (1966) and MS in pharmacognosy (1969) from Idaho State University. He then earned his PhD in pharmacognosy from the University of Washington in 1972. Keller was appointed shortly thereafter to the faculty of the School of Pharmacy at Northeast Louisiana University (NLU; now the University of Louisiana at Monroe) in Monroe, Louisiana, where he was employed for more than 20 years. He became head of the Division of Pharmaceutics and Medicinal Chemistry in 1978 and was named Clarke Williams Distinguished Professor at NLU in 1989. In 1995, Keller moved to the McWhorter School of Pharmacy at Samford University in Birmingham, Alabama, as professor and chair of the Department of Pharmaceutical Sciences.

In April 2001, Keller transitioned from academia to working at a major botanicals company when he became vice president of health sciences and educational services and chief scientific resource officer at Nature's Sunshine Products, Inc. (NSP) based in Spanish Fork, Utah. During the industrial part of his career, he worked initially for several years with Jerry McLaughlin, PhD, former ASP president and former professor of pharmacognosy at Purdue University. At the University of Washington, McLaughlin previously had been Keller's doctoral dissertation advisor on the investigation of cactus alkaloids. Keller was highly regarded by the senior management of his company and was appointed to the NSP Medical and Scientific Advisory Board in 2014. Though he formally retired in 2015, Keller remained on this advisory board for some time thereafter.

In addition to being secretary of ASP, Keller was a member of the Board of Trustees of the American Herbal Products Association and was on the Dean's Advisory Board of the colleges of pharmacy at Idaho State University and Texas A&M University. While in academia, Keller served on several National Institutes of Health grant review panels and was a frequent journal manuscript reviewer. He published about 100 journal articles and made approximately 200 scientific addresses both in the United States and internationally. In the 1990s, Keller spent a sabbatical period as a guest professor in the Department of Pharmacy at the Swiss Federal Institute of Technology (ETH-Zurich) in Zurich, Switzerland, where he worked with ASP Honorary Member Professor Otto Sticher, PhD. Keller became an honorary member of ASP in 2010.

In 2002, Keller approached me about performing some phytochemical and biological testing laboratory support work on selected botanical dietary ingredients. We started off by looking at noni (*Morinda citrifolia*, Rubiaceae), and, over the years, my group went on to also investigate açaí (*Euterpe oleracea*, Arecaceae), black chokeberry (*Aronia* spp., Rosaceae), goji berry (*Lycium chinense* and *L. barbarum*, Solanaceae), mangosteen (*Garcinia mangostana*, Clusiaceae), licorice (*Glycyrrhiza glabra*, Fabaceae), and maqui berry (*Aristotelia chilensis*, Elaeocarpaceae). This collaborative work between Keller and my group at Ohio State University (OSU) eventually led to 11 journal articles and 18 meeting presentations on these topics. This gave an opportunity for several of my former graduate students at OSU to perform in-depth research on botanical dietary ingredients. Having a research program on botanical dietary supplements gave me useful insight for teaching professional pharmacy students. Thus, my past collaboration with Keller was extremely helpful from the standpoint of both research and teaching.

Mark Blumenthal, American Botanical Council founder and executive director, said: "I knew Bill from our membership in ASP and, later, we increased our communication and friendship when he was working on research and education at Nature's Sunshine Products, a long-established major herb business. Like many of his friends and colleagues, I consider Bill a deeply humble, decent, kind, and generous person, and I will always appreciate his strong support for the educational mission of ABC."

Ill health caused Keller to resign in 2015 from both his herb industry job and his position as the longest-serving secretary of ASP. Bill Keller is survived by his second wife, Tram Nguyen; two sons, Jeffrey and Scott; two grandsons; and numerous friends and professional colleagues. HG

***A. Douglas Kinghorn, PhD, DSc**, is the Jack L. Beal Chair and Distinguished Scholar Awardee in the College of Pharmacy at the Ohio State University. He served as ASP president from 1990 to 1991, is an honorary member of ASP, and the emeritus editor of the* Journal of Natural Products.

This memorial was edited and shortened from a longer tribute by Kinghorn that was published in the Winter 2020 edition of the ASP newsletter (Volume 56, Issue 4).

FOOD AS MEDICINE
POMEGRANATE

Pomegranate *Punica granatum*. Photo ©2021 Steven Foster

Pomegranate fruit (*Punica granatum*, Lythraceae) has a millennia-old history in folklore, mythology, art, and medicine. Often considered a cure-all in the traditional medicine systems of Greece, Rome, and Asia, including India, the ruby red pomegranate seeds were equally revered for their sweet-tart flavor in both sweet and savory cooking applications. Currently, pomegranate juice and extracts are being researched for their efficacy in a variety of conditions, including metabolic disorders, cardiovascular disease, and others.

Nutrition Profile

Per 100 grams (~3/4 cup) of pomegranate seeds

Very good source of		
Vitamin K	16.4 mcg	13.7% DV
Dietary Fiber	4.0 g	13% DV
Vitamin C	10.2 mg	11% DV
Good source of		
Folate	38 mcg	9.5% DV
Thiamin	0.07 mg	5.8% DV
Potassium	236 mg	5% DV
Also provides		
Vitamin B_6	0.08 mg	4.7% DV
Riboflavin (B_2)	0.05 mg	3.8% DV
Zinc	0.35 mg	3.2% DV

Fast Facts

- The number of seeds inside a pomegranate can vary from 200 to 1,400 based on fruit size and variety. An average-sized pomegranate contains approximately 600 seeds.
- Native to the region of Persia, pomegranate is an ancient cultigen that has been cultivated and naturalized throughout the Mediterranean region for more than 5,000 years.
- In Ayurvedic medicine, the pomegranate is considered "a whole pharmacy unto itself" and is specifically indicated to treat parasites, ulcers, and diarrhea.
- Clinical studies have demonstrated that pomegranate's potent antioxidant and anti-inflammatory effects may help reduce risk of heart disease, diabetes, arthritis, and some cancers.

Phytochemical Focus

- All parts of the pomegranate contain polyphenols, naturally occurring compounds that reduce oxidative stress and inflammation.
- The fruit's intense red color indicates the presence of abundant anthocyanins — the largest and most important group of flavonoids present in pomegranate arils and juice.

About ABC's Food as Medicine Series

Every other month, the American Botanical Council's monthly e-newsletter HerbalEGram highlights a conventional food and explores its history, traditional uses, nutritional profile, and modern medicinal research. The articles, written by ABC Education Coordinator Jenny Perez, also feature a nutritious recipe to encourage readers to experience the extensive benefits of these whole foods.

The full "Food as Medicine: Pomegranate" article with references is available on ABC's website in the HerbalEGram section (January 2021 issue).

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