HerbalGram 117 • Feb – April 2018

Ivy Leaf Systematic Review • Psyllium Profile • Tulsi Research Review
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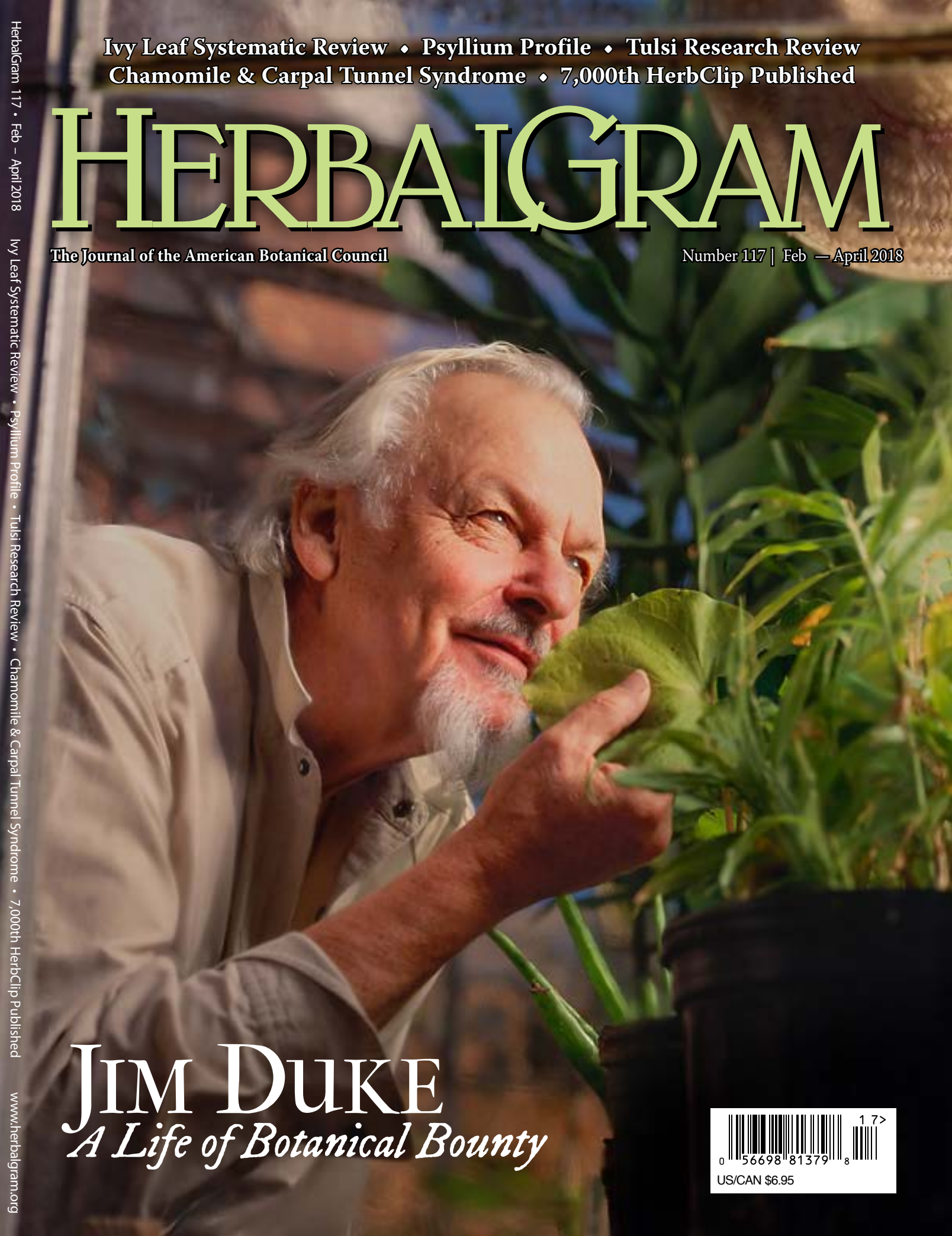

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# dear *reader*

## Remembering Jim Duke

The worlds of ethnobotany and herbal medicine have lost one of their truest and strongest champions with the passing of Jim Duke, PhD, at age 88 in December 2017. Jim was one of the most prolific and influential people in the modern herbal medicine scene and was respected by scientists, herbalists, and the many thousands of readers of his books and articles.

I met Jim at the first Herb Trade Association symposium in Santa Cruz, California, in the spring of 1977. Over the years, he sent me large manila envelopes full of photocopied botanical research articles from the US Department of Agriculture (USDA) addressed to "Dr. Mark Blumenthal" so he could use the USDA's franking privileges (free mail for government employees). Jim was the first person who consistently, and jokingly, referred to me as "Doctor." (I do not have a formal advanced degree, like many of my herbal brothers and sisters.) Jim was one of my most influential mentors and exhibited a passion for all vascular plants, their myriad properties, and their countless benefits for indigenous peoples as well as those in developed societies — the stuff of ethnobotany.

I am profoundly grateful to have known and learned from him, and that he supported my efforts to start and build ABC. He was one of the first three board members when ABC was founded in November 1988, along with the late Professor Norman Farnsworth, PhD, a respected pharmacognosist, and me. (The esteemed Professor Varro Tyler, PhD, joined the board a few years later.) Until his passing, Jim remained on the ABC Board of Trustees as the Director Emeritus, or "Director Demeritus," as he frequently referred to it in his usual way of wryly twisting language.

We took numerous trips together to the Peruvian Amazon and Andean highlands, as well as Belize, Costa Rica, Kenya, and South Africa. We even found ourselves hanging out in Seoul, South Korea, at the 3rd International Ginseng Symposium in 1980.

I have so many fond memories of Jim; here are but a few:

His singing and playing a beat-up Spanish guitar in the screened-in bar at Explorama Lodge on the Amazon, downriver from Iquitos, Peru. (On many trips to Amazonia, he would take a beat-up acoustic guitar and leave it there for the locals.)

Drinking the crude *aguardiente* rum distilled from the fermented sugarcane juice, which was squeezed out of the *caña* (sugarcane) by a primitive press powered by an ox that tread a well-worn circular path on the bank of the Amazon near Explorama.

Eating *suri* — the nutritious larvae of the South American palm weevil — at a rustic, no-frills camp on the Napo River. (Being omnivorous, he ate the suri; being vegetarian, I did not.)

His "Dukeisms": Jim's well-known wordplay (e.g., as in the double entendre "Herbalbum," his anthology of "Varicose Verse," and his book *Lewd Latin Lexicon*) and stream-of-consciousness emails (Steven Foster, an inveterate and unrepentant archivist, has collected hundreds of them). He penned articles for *HerbalGram* when it was still a newsletter in the early- to mid-80s, and I enjoyed the challenge of editing his often-poetic prose.

We extend our deep gratitude to Helen Lowe Metzman for her contribution to this issue, and to Jim's life. Helen is the chief gardener at Jim and his wife Peggy's six-acre Herbal Vineyard at their home in rural Maryland, and was Jim's right-hand helper for the past decade. The day after Jim passed over, Helen sat down at his desk and wrote a heartfelt tribute on his old desktop computer. We include Helen's account in our special section devoted to Jim.

To provide a detailed insight into Jim's professional life and publications, Steven Foster, botanist, author, and co-author of one of Jim's most popular books (*Peterson Field Guide to Medicinal Plants and Herbs of Eastern and Central North America*) has written what will no doubt become *the* definitive summary of Jim's many botanical accomplishments. Included in Steven's compelling 7,000-plus-word article is the story of how Jim documented the potential adverse effects of the proposed use of nuclear weapons in the 1960s to create a new Panama Canal on the plants, environment, and native peoples of the region. Jim spent a considerable amount of time in Panama inventorying the plants of the rainforest and befriending the local people.

I've never known anyone like Jim Duke, and I know that my life and the lives of so many others who respected, admired, and loved him are immensely richer for having known him. Whether you knew Jim or not, you will enjoy reading Helen and Steven's tributes to him in our 18-page spread with colorful photos and stories of the man who helped propel herbal medicine in ways that can never be fully measured. HG

Mark Blumenthal

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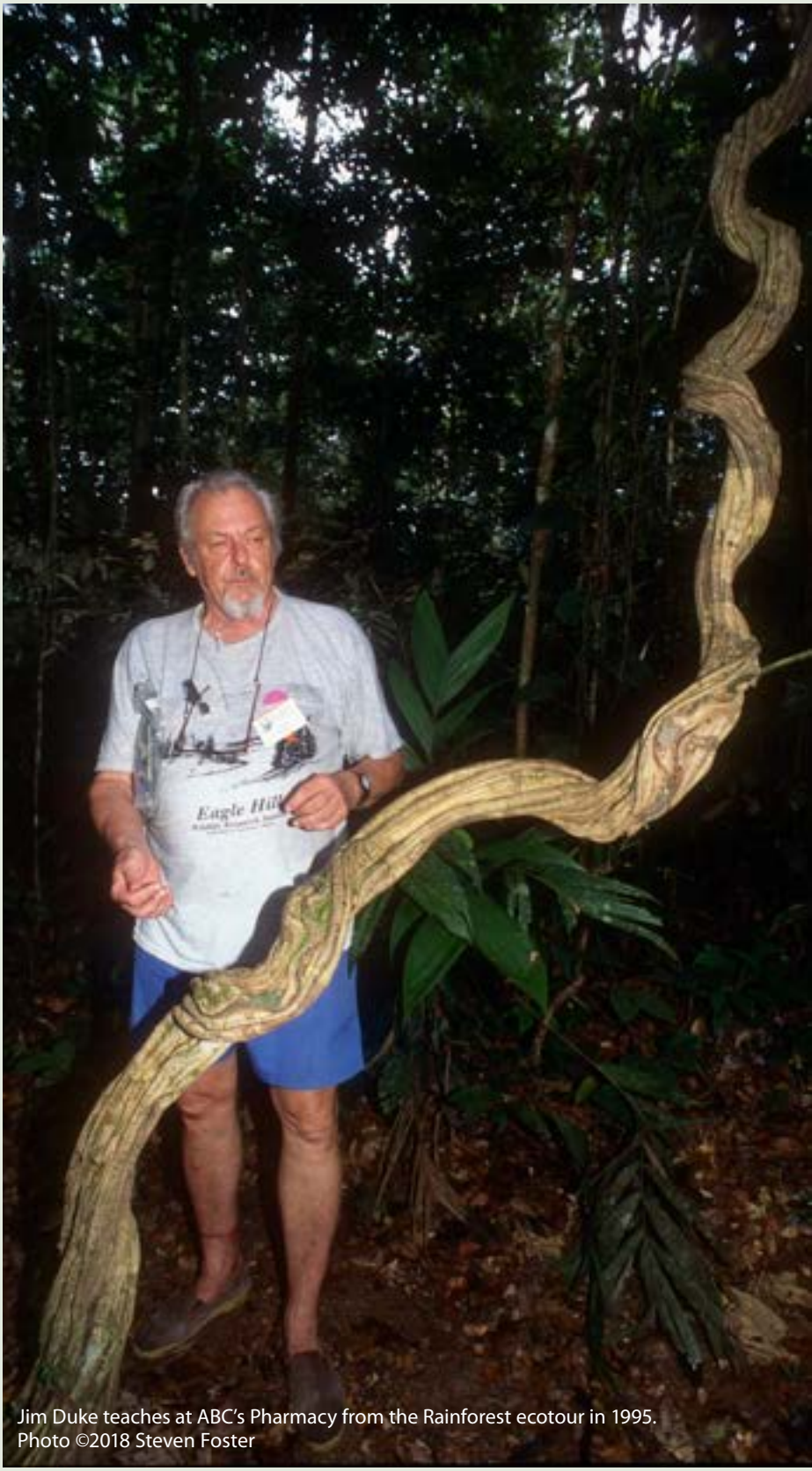

Jim Duke teaches at ABC's Pharmacy from the Rainforest ecotour in 1995.
Photo ©2018 Steven Foster

# departments



**On the Cover**
James A. Duke, PhD. Photo ©2018 Sam Kittner




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# Psyllium

***Plantago ovata* (*P. ispaghula*), *P. afra* (*P. psyllium*), and *P. indica* (*P. arenaria*)**

Family: Plantaginaceae

## INTRODUCTION

The genus *Plantago* comprises about 200 species,[1] with 56 subspecies, 33 forms, one subform, 188 varieties, and nine subvarieties.[2]

The species commonly called psyllium are important because of their highly mucilaginous seeds. An herbaceous plant, psyllium has opposite leaves with a midrib as its primary venation, smooth or slightly toothed margins, and pubescent stems. Flowers are borne on a spike, are green or white, and produce a seed capsule with two seeds each.[3]

The center of diversity for *Plantago* species is believed to be central Asia, although some species are now widely dispersed,[4] including 10 species in India,[5] 21 in Egypt,[6] and 21 in Turkey.[2] There are at least 12 Iranian endemic *P. ovata* ecotypes.[7] Although occurring rarely, *P. afra* is found in the Mediterranean region of southern Europe, northern Africa (Egypt), and western Asia (Jordan, Syria, and Turkey). In Egypt, *P. afra* is distributed in the Sahara Desert east of the Nile River in the Red Sea region, Gebel Elba region, and Sinai region.[6] *Plantago ovata*, native to the Mediterranean region and western Asia,[8] occurs in the wild mainly in desert regions of the Northern Hemisphere between the 26th and 36th latitudes,[9] from northern Africa to parts of the Arabian Peninsula,[6] to the central Asian deserts of Kyzyl Kum (Turkmenistan) and parts of southern Asia (Afghanistan, Iran, and Pakistan).[10] It was introduced to India via the settlement of Arab Muslims on India's west coast during the Middle Ages.[11]

Currently, western India (Gujarat and Rajasthan) is the world's largest psyllium-producing region, with a cultivation area of about 60,000 hectares (148,263 acres).[10] *Plantago ovata* is also cultivated in Iran.[12] Although much of the literature claims that *P. ovata* is the only commercially cultivated species of the genus,[4] *Flora of China* states that *P. indica* (syn. *P. arenaria*), which is native to northern Africa, parts of Europe, southwestern Asia, and central Asia (Kazakhstan, Kyrgyzstan, and Tajikistan), is cultivated in several provinces of China for its medicinal seeds.[13]

Although the psyllium of global commerce is supplied almost entirely by *P. ovata* from India, the seeds and seed coats (husks) of three species are monographed in national pharmacopeias and therapeutic compendia under various common names, including psyllium, ispaghula, and/or plantago, depending on the country. For example, the *European Pharmacopoeia* (PhEur) defines "Psyllium seed" as the ripe, whole, dry seeds of *P. afra* (syn. *P. psyllium*) or *P. indica* (syn. *P. arenaria*), while describing the dried, ripe seeds of *P. ovata* (syn. *P. ispaghula*) as "Ispaghula seed."[14] On the other hand, the *United States Pharmacopeia* (USP) defines "Plantago seed" as the cleaned, dried, ripe seed of *P. psyllium* or *P. indica* (syn. *P. arenaria*), known in commerce as Spanish or French psyllium; or *P. ovata*, known in commerce as blond psyllium or Indian plantago seed. Furthermore, USP defines "Psyllium husk" as the cleaned, dried seed coat (epidermis) separated by winnowing and threshing from the seeds of *P. ovata*, known in commerce as blond psyllium, Indian psyllium, or ispaghula; or of *P. arenaria* (syn. *P. psyllium*), known in commerce as Spanish or French psyllium.[15] The different official compendia give different preferences as to which Latin binomial is accepted and which is a synonym, which potentially makes the nomenclature confusing when comparing pharmacopeial standards.

## HISTORY AND CULTURAL SIGNIFICANCE

The many similarly spelled common names used for *P. ovata* in India (isabgol, isabgul, isapghul, isobgul, ispaghula, and isubgol) are derived from the Persian words *isap* and *ghol*, meaning "horse ear," which refers to the shape of the seed.[16] The Latin term *psyllium* stems from the Greek *psulla* meaning "flea," which refers to the flea-like size, shape, and color of the seed.[8] French botanist Joseph Pitton de Tournefort (1656-1708) described several species of the genus *Plantago* in his book *Institutiones rei herbariae*, published in 1700, although none of the species mentioned in his text are the subject of this article.[17] In his 1753 publication *Species Plantarum*, Swedish botanist Carl Linnaeus (1707-1778) listed 16 *Plantago* species, including *P. psyllium*, stating its habitat as southern Europe, and *P. cynops*, stating its habitat as India.[18] *Plantago cynops* is now considered a synonym of *P. afra*. In his 1759 *Systema Naturae*, Linnaeus added *P. indica*,[19] with an epithet and references that suggested a habitat much further east than Europe.[20]

Indian government ministries have established standards for the various grades and qualities of psyllium produced in India. In addition to the "Ispaghula husk" monograph of the *Indian Pharmacopoeia* (an institution of the Ministry of Health and Family Welfare),[21] India's Ministry of Agriculture established three distinct "AGMARK" grade designations in 1982 that defined the quality of psyllium seed husk (Isubgol Husk Grade I, Grade II, and Grade "Special").[22] In 2006, the National Multi-Commodity Exchange of India Ltd. (NMCE), governed by the Ministry of Finance, introduced isabgol seed futures (agreements to buy or sell isabgol at a specific date in the future at a set price through a government-regulated commodity exchange) into its commodity trading system, which also established quality specifications and compliance requirements as terms of the futures contracts.[23]

Psyllium ingredients are differentiated by grade designations according to purity (e.g., 95% purity), which correspond to specific uses and minimum effective doses (e.g., the percentage of pure husk and the swelling index corre-

**Psyllium**
*Plantago ovata*
Photo ©2018 Steven Foster

spond to efficacy as a laxative). Indian exporters generally specify at least seven different purity grades (70%, 80%, 85%, 90%, 95%, 98%, and 99%). The 70% purity grade, known as "Industrial Grade Kha-Kha Powder" or "Psyllium Industrial Dust," is a byproduct used mainly as horse feed and in veterinary medicines, but also in landscaping to prevent soil erosion.[24] Other post-processing byproduct grades include "Lali" and "Golaisab," both used as cattle feed; "Chito," used as pig feed; and "Khakho," used to prevent slipping on ice.[16] The 80%, 85%, and 90% grades are used mainly as food additives, pharmaceutical aids (excipients), and/or dietary supplement ingredients, respectively. Purity grades of 95%, 98%, and 99%, the therapeutic grades generally conforming to pharmacopeial quality standards, are used mainly as bulk-forming laxative active ingredients or as soluble fiber supplement ingredients.[24]

In 1975, the US Food and Drug Administration (FDA) proposed the establishment of monographs for nonprescription, over-the-counter (OTC) laxative, antidiarrheal, emetic, and antiemetic drug products that listed various psyllium substances (e.g., plantago seed, psyllium seed, psyllium seed husk, psyllium hemicellulose, and psyllium hydrophilic mucilloid) as safe and effective bulk-forming laxative active ingredients for short-term relief of constipation.[25] Bulk-forming laxatives are agents that increase bulk volume and water content of the stool, thereby promoting bowel movement. Ten years later, in 1985, the FDA published a tentative final monograph for OTC laxative drug products listing the same psyllium ingredients with dosage and labeling statement requirements.[26] The following year, the FDA amended the tentative final monograph by modifying the directions for the use of bulk laxatives.[27] In 1992, the FDA reopened the monograph to include new data on the combination of psyllium and bran laxative active ingredients.[28] In 2007, the FDA again amended the laxative monograph in order to remove the granular dosage form of bulk-forming psyllium ingredients for safety reasons (risk of choking). This rule did not apply to psyllium laxatives in nongranular dosage forms such as powders, tablets, or wafers.[29]

Because it is a requirement that OTC drug active ingredients adhere to USP quality standards, there are official monographs for "Plantago Seed USP" (dried, ripe seed of *P. psyllium*, *P. indica*, or *P. ovata*), "Psyllium Hemicellulose USP" (alkali-soluble fraction of the husk from *P. ovata*), "Psyllium Husk USP" (seed coat from the seeds of *P. ovata*, *P. arenaria*, or *P. psyllium*), and "Psyllium Hydrophilic Mucilloid for Oral Suspension USP" (dry mixture of Psyllium Husk USP with suitable additives). In 1998, the FDA decided to authorize certain health claims on the association between soluble fiber from psyllium seed husk and reduced risk of coronary heart disease (CHD).[30] Furthermore, in 2000, the FDA ruled that certain OTC drug monograph claims, including claims listed in its laxative drug monograph, would now also be acceptable structure/function claim statements for dietary supplement products. In particular, this included the claim "for the relief of occasional constipation," because occasional constipation is not a characteristic symptom of a disease.[31] This led to the remarkable situation in which psyllium-based OTC drug products and dietary supplement products could now be labeled and marketed with the same claim statement. And, due to the newly FDA-authorized health claim, some psyllium product labels began to carry both a "Drug Facts" box and a "Supplement Facts" box because different dosage, instructions, and other labeling statements applied depending on whether the product was intended to be used as an OTC laxative drug or as a dietary supplement for heart health.

In 1985, the German Commission E approved the use of "Black Psyllium Seed" (*P. afra* and/or *P. indica*) as a nonprescription medicine for treating chronic constipation and irritable bowel. Subsequently, in 1990, the Commission E approved the use of both "Blond Psyllium Seed" (*P. ovata*) and "Blond Psyllium Seed Husk" for treating "chronic constipation; disorders whereby easy bowel movements with a loose stool are desirable, e.g., in patients with anal fissures, hemorrhoids, following anal/rectal surgery; during pregnancy; as a secondary medication in the treatment of various kinds of diarrhea and in the treatment of irritable bowel."[32] Since then, national labeling standards monographs of European Union (EU) member states, such as those of the German Commission E, have been superseded by monographs of the European Medicines Agency (EMA).

In 2006, the EMA published labeling standards monographs for "Psyllii semen" (seed of *P. afra* or *P. indica*),[33] "Plantaginis ovatae seminis tegumentum" (seed coat of *P. ovata*),[34] and "Plantaginis ovatae semen" (seed of *P. ovata*)[35] (which were superseded by revised monographs in 2013), applicable when used as active ingredients of licensed well-established use herbal medicinal products (WEU-HMPs) in the EU. Correspondingly, the European Directorate for the Quality of Medicines (EDQM) published quality standards monographs in the PhEur for "Ispaghula Husk PhEur" (episperm and collapsed adjacent layers removed from the seeds of *P. ovata*), "Ispaghula Seed PhEur" (dried ripe seeds of *P. ovata*), and "Psyllium Seed PhEur" (ripe, whole, dry seeds of *P. afra* or *P. indica*).[14] In 1999, a comprehensive monograph (quality and therapeutics) for "Semen Plantaginis" (dried, ripe seed of *P. afra*, *P. indica*, *P. ovata*, or *P. asiatica*) was included in volume one of the *WHO Monographs on Selected Medicinal Plants*.[36] A subsequent monograph for "Testa Plantaginis" (epidermis and collapsed adjacent layers removed from the seeds of *P. ovata*) entered volume three of the *WHO Monographs on Selected Medicinal Plants* in 2007.[37]

## CURRENT AUTHORIZED USES IN COSMETICS, FOODS, AND MEDICINES

In India, "Ispaghula" is listed in the National List of Essential Medicines and monographed in the *National Formulary of India* as a laxative drug indicated for treatment of constipation and irritable colon syndrome.[38] In the United States, the FDA classifies selected defined psyl-

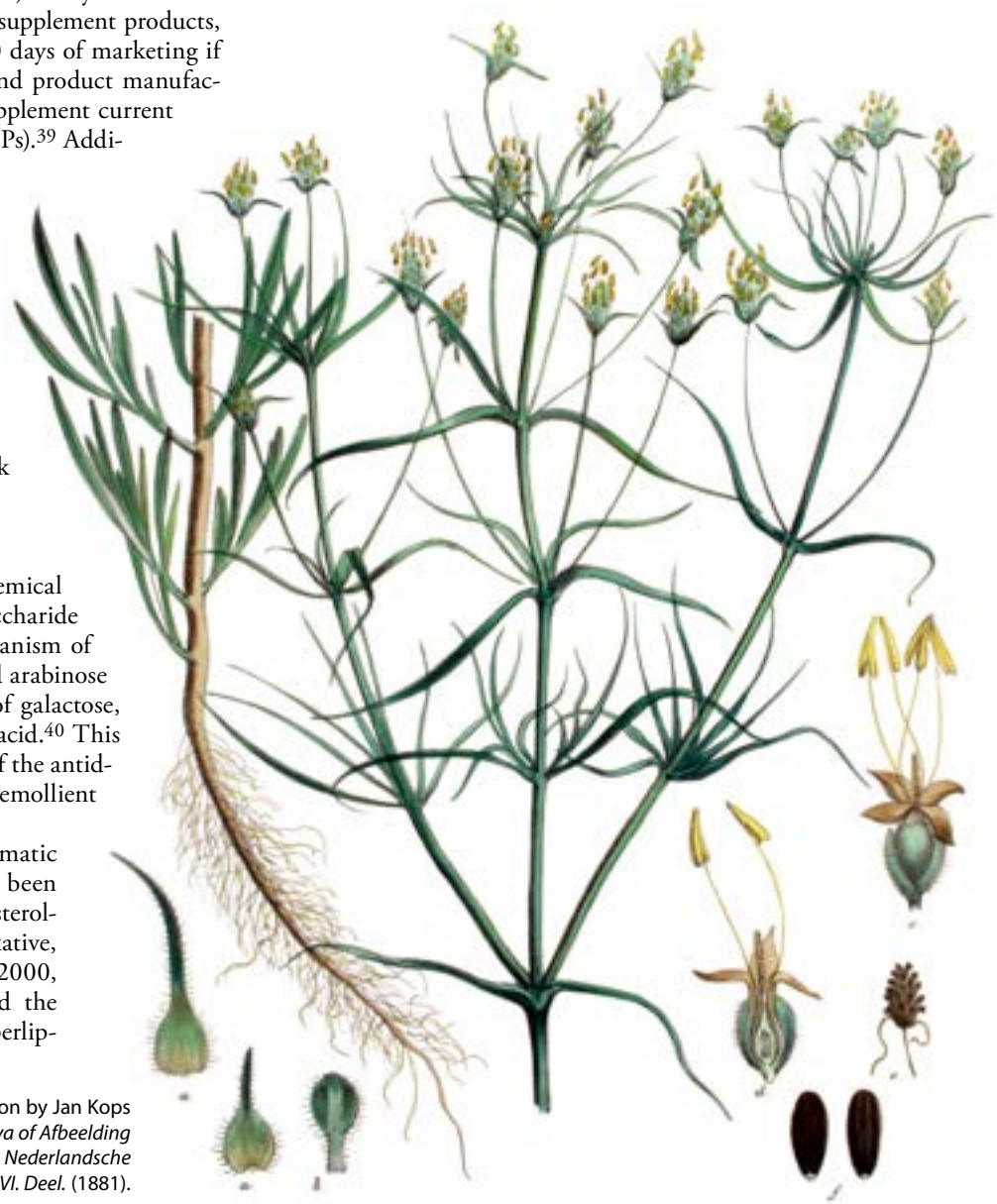
lium substances (Plantago Seed USP, Psyllium Hemicellulose USP, Psyllium Husk USP, and Psyllium Hydrophilic Mucilloid for Oral Suspension USP) as Generally Recognized as Safe and Effective (GRASE) bulk-forming active ingredients of laxative drug products. The permitted indication for use statement is "for relief of occasional constipation," which may be followed by the word "irregularity." Psyllium Husk USP may also be used in combination with another bulk-forming laxative active ingredient, Malt Soup Extract, which is obtained from partially germinated grain of one or more varieties of barley (*Hordeum vulgare*, Poaceae) that contain amylolytic enzymes. FDA also permits Psyllium Hemicellulose USP to be used in combination with the stimulant laxative active ingredient Sennosides USP (a partially purified natural complex of anthraquinone glucosides isolated from senna [*Senna alexandrina*, Fabaceae] leaflets and/or pods).[26] Psyllium is also permitted as a component of dietary supplement products, requiring FDA notification within 30 days of marketing if a structure/function claim is made and product manufacturing that conforms with dietary supplement current Good Manufacturing Practices (cGMPs).[39] Additionally, food supplement products that provide 7 g or more per day of soluble fiber from psyllium seed husk, of a purity of no less than 95% as required in the Psyllium Husk USP monograph, may be labeled with an FDA-authorized health claim to the effect of: "Soluble fiber from foods such as psyllium husk, as part of a diet low in saturated fat and cholesterol, may reduce the risk of heart disease."[30]

## MODERN RESEARCH

*Plantago* species have complex chemical profiles, but the mucilaginous polysaccharide responsible for psyllium's main mechanism of action is primarily made of xylose and arabinose (arabinoxylan), with small amounts of galactose, glucose, rhamnose, and galacturonic acid.[40] This mucilage is thought to provide most of the antidiarrheal, laxative, demulcent, and emollient effects of psyllium.

Numerous clinical studies, systematic reviews, and meta-analyses have been conducted on psyllium for its cholesterol-lowering, blood pressure-lowering, laxative, and related effects. Prior to the year 2000, at least eight clinical studies showed the efficacy of psyllium for treating hyperlipidemia alone.

Two meta-analyses and one systematic review support the beneficial effects of psyllium supplementation on blood lipids. In a 1997 meta-analysis of 12 studies on 404 adults with mild-to-moderate hypercholesterolemia, it was shown that subjects who ate a psyllium-enriched cereal (≤ 3 g soluble fiber/day; species not stated) experienced lowered total cholesterol (TC; a 5% reduction) and low-density lipoprotein cholesterol (LDL-C; a 9% reduction) but not high-density lipoprotein cholesterol (HDL-C).[41] A 2014 systematic review of 232 more recent studies also demonstrated the cholesterol-lowering effects of eating psyllium-enriched cereal, adding that improved glucose or insulin responses were seen in diabetic patients who ate high-fiber, psyllium-based cereals compared with regular cereals.[42] A meta-analysis published in 2000 excluded studies on psyllium-enriched cereals



*Plantago indica* Illustration by Jan Kops (1765-1849) from *Flora Batava of Afbeelding en Beschrijving van Nederlandsche Gevassen, XVI. Deel.* (1881).

and focused on studies in which subjects supplemented a low-fat diet with 10.2 g psyllium per day for eight or more weeks. Pooled data on 656 subjects in eight studies showed that psyllium significantly lowered TC by 4% and LDL-C by 7%.[43]

One randomized, double-blind, placebo-controlled, parallel clinical trial in 2014 evaluated the effects of psyllium on 51 children and adolescents (6-19 years old) with mild-to-moderate hypercholesterolemia. All subjects followed the National Cholesterol Education Program (NCEP) Step 2 diet (55% of calories as carbohydrates, 15% as protein, less than 30% as fat [less than 7% as saturated fatty acids], and less than 200 mg cholesterol daily) for six weeks. After two weeks, they were randomly assigned to take either 7 g of psyllium from *P. ovata* (Laxofibra [3.5 g hydrophilic mucilloid/5 g powder]; Almeida Prado Pharmaceutical Laboratory; São Paulo, Brazil) twice daily or placebo. At eight weeks, mean TC and LDL-C concentrations in the psyllium group were 6.7% and 11% lower than baseline values, respectively. Lipid profiles of the psyllium group were also significantly lower than those of the placebo group at eight weeks, but no significant changes were observed in the psyllium group in triglyceride or HDL-C concentrations, or in the LDL-C:HDL-C ratio. Additionally, normal cholesterol values were achieved in six (23%) of the 26 subjects in the psyllium group.[44]

Strangely, while the relief of constipation is one of the primary uses of psyllium, few high-quality clinical studies have investigated this use, and none thus far in the 21st century, as revealed in two meta-analyses conducted in 2012 and 2014.[45,46] One of the few randomized, double-blind studies that evaluated psyllium for its benefits in chronic constipation compared it with docusate sodium and was published in 1998. After a two-week baseline placebo phase, subjects (N = 170, 20-70 years old) with chronic idiopathic constipation were randomly assigned to take 5.1 g psyllium (Smooth Texture Sugar-Free Orange-Flavored Metamucil; Procter & Gamble; Cincinnati, Ohio) plus docusate sodium placebo twice a day for two weeks or 100 g docusate sodium plus psyllium placebo. At the end of weeks one and two, the psyllium group showed a significant increase in stool water content (2.33% at the end of the treatment phase), corresponding to softer stools, compared to the docusate sodium group (0.01% at the end of the treatment phase). This effect started three days after initiation of treatment and increased over the treatment period. Additionally, in week two, psyllium increased stool output better than docusate sodium (359.9 g/week versus 271.9 g/week, respectively), and bowel movement (BM) frequency (3.5 BMs/week versus 2.9 BMs/week, respectively).[47]

A 2017 randomized, double-blind study investigated the effects of psyllium on abdominal pain and stool patterns in children with irritable bowel syndrome (IBS). After two weeks eating their normal diet followed by an eight-day diet that excluded carbohydrates (which are thought to cause IBS symptoms), children (7-18 years old)

who did not experience ≥ 75% improvement in abdominal pain continued to the treatment phase. Subjects were randomly assigned to take psyllium (6 g for children 7-11 years old, 12 g for children 12-18 years old; Konsyl Pharmaceuticals; Easton, Maryland; no other information provided) or placebo for six weeks. Outcomes were measured by pain/stool diaries, breath hydrogen/methane, gut permeability, and microbiome composition. After treatment, the psyllium group experienced a significant reduction in pain compared to placebo (mean reductions of 8.2 ± 1.2 versus 4.1 ± 1.3, respectively, per the Numerical Rating Scale [NRS-11]). There were no significant changes in the other measurements between groups.[48]

In 2018, a systematic review and meta-analysis reviewed randomized controlled trials that evaluated the effect of viscous soluble fiber (VSF) on blood pressure. Studies were included if they addressed the effects of VSF supplements (psyllium, β-glucan, guar gum, konjac [*Amorphophallus konjac*, Araceae], or pectin) or diets enriched with VSF on systolic blood pressure (SBP) or diastolic blood pressure (DBP), had a follow-up period of at least four weeks, and used fiber from a single source so that differences between fiber types could be evaluated. A total of 22 studies were reviewed, and the authors concluded that supplementation with VSF, particularly psyllium, can have a modest but statistically significant effect on lowering SBP and DBP, and that their review was the first to show that psyllium can significantly lower SBP.[49]

Since controlling hunger between meals is a challenge for some individuals trying to change their eating habits, Brum et al. (2016) investigated the effects of psyllium on satiety in two sequential randomized, double-blind, placebo-controlled, crossover design studies. In the first study, healthy subjects (N = 30, 18-55 years old) took 3.4 g or 6.8 g Metamucil in 295.7 mL water or placebo before breakfast and lunch for three days, or 10.2 g before breakfast only for three days. Meals were provided based on estimated individual energy requirements. Significant mean reductions in hunger and desire to eat and increased fullness between meals were experienced with all three doses compared to placebo, with the 6.8 g dose resulting in the most consistent satiety. In the second study, subjects (N = 44) took 6.8 g Metamucil in 295.7 mL water or placebo before breakfast (energy-restricted) and lunch on days one and two, and before breakfast (energy-restricted) only on day three. While the psyllium group experienced statistically significant reductions in mean hunger and desire to eat and increased fullness over three days compared to placebo, the satiety was less than in the first study.[50]

## FUTURE OUTLOOK

In the 2015-2016 agricultural year (April to March), India exported 38,055,580 kg (83,898,193 lbs) of psyllium husk and 1,552,530 kg (3,422,743 lbs) of psyllium seed. In the subsequent crop year 2016-2017, India

**Psyllium** *Plantago ovata* Photo ©2018 Steven Foster

exported 35,422,980 kg (78,094,303 lbs) of husk and 1,005,170 kg (2,216,021 lbs) of seed. On average, the United States imports about 45% of India's total annual psyllium husk export quantity, and most of the remainder is imported by Germany, Italy, Mexico, Pakistan, the United Kingdom, Belgium, Malaysia, Australia, France, and China.[51] More than 99% of psyllium husk imported by the United States originates from India.[52] The main importers of Indian psyllium seed, however, are Germany, Iran, Sweden, Pakistan, and the United Arab Emirates.[51]

Based on data from the past five years, the United States imports an average of about 16,270,080 kg (35,869,386 lbs) of psyllium husk annually, placing psyllium among the top medicinal plants imported and used in the United States. (For comparison, in 2016, the United States imported about 542,000 kg [1,194,905 lbs] of ginseng [*Panax* spp., Araliaceae] root from China, Canada, and South Korea).[52] The significant use of psyllium is not quantified in the various annual market surveys that rank herbal dietary supplement consumption in the United States,[53] likely because most psyllium products are labeled and marketed as OTC botanical drug products, although many are labeled as both OTC drugs and fiber supplement products.

**Psyllium** *Plantago ovata* Photo ©2018 Steven Foster

India dominates the world market in the production and export of psyllium ingredients. Some of the main buyers include the Procter & Gamble Company (Metamucil), Morepen Laboratories Ltd. (Dr. Morepen Fibre-X Sat Isabgol),[8] Konsyl Pharmaceuticals (Konsyl Original Formula), and Madaus GmbH (Agiolax), among others.[54] Of India's total psyllium production, about 75% of the crop from Gujarat state and about 90% of the crop from Rajasthan state is exported. About 93% of the crop exported from Gujarat and Rajasthan is psyllium husk. There are about 70 Indian companies that export psyllium husk and seed, with the leading processors and exporters based in Sindhpur in the Mehsana district and in Palanpur in the Banaskantha district of Gujarat state.[8]

According to Batanouny (1999), *P. afra* is endangered in Egypt due to habitat loss. Although there is some cultivation, the species is in need of ex situ conservation.[6] The International Union for Conservation of Nature (IUCN) European Red List of Medicinal Plants assigns *P. afra*, *P. indica* (syn. *P. arenaria*), and *P. ovata* to the conservation category of least concern (LC), meaning that these *Plantago* species are not threatened in Europe.[55]

Lal et al. (2009) reported an

urgent need to collect more variability from both wild and cultivated populations of *P. ovata* (i.e., diverse genotypes must be collected, evaluated, and used for direct introduction in cultivation or as parents for conservation and crop improvement purposes). It is predicted that the rapid replacement of *P. ovata* landraces (domesticated, locally adapted, traditional varieties) by highly uniform varieties will continue, leading to an eventual disappearance of genetic resources that have adapted over hundreds of years.[11] There are at least six high-yielding varieties of *P. ovata* cultivated in India, including *P. ovata* var. "Jawahar Isabgol 4" available from the Medicinal and Aromatic Plant (MAP) unit at the College of Horticulture, Mandsaur in Madhya Pradesh and *P. ovata* var. "Niharika" released by the Central Institute of Medicinal and Aromatic Plants (CIMAP) in Lucknow, Uttar Pradesh.[8]

The genetic diversity of psyllium crops is a major concern to some plant breeders and germplasm curators. In a study to determine the genetic diversity and relationships among 38 genotypes of seven *Plantago* species in India, a diversity analysis using phenotypic and molecular markers showed that the seven species were significantly different from each other but variability within *P. ovata* was very limited. The authors suggest that induced mutation could be used to widen the range of variation in breeding strategies to improve crop yield and disease resistance.[56] Since *P. ovata* is an introduced crop in India, productivity has been constrained by biotic stress (caused in plants due to damage instigated by other living organisms) and abiotic stress (caused in plants by drought, flooding, extreme temperatures), leading to heavy losses in quality and yield.

Crop improvement has been difficult due to limited genetic resources. Some agronomists suggest that among the approximately 200 wild crop relatives of *P. ovata* there exists a reservoir of important genes that they believe, if introgressed to cultivated *P. ovata* through marker-assisted breeding, could lead to genetic improvement of the crop.[57] Introgression is the incorporation (usually via hybridization and backcrossing) of alleles (a variant form of a gene) from one species into the gene pool of a second, divergent species.[58] Research to characterize the genetic variability of wild *P. ovata* genotypes that occur in southern Iran is also being carried out for the purpose of breeding new varieties.[59]

Given its almost global regulatory status as an essential, safe, and effective medicine for relief of constipation and as a good source of soluble fiber for heart health, annual demand for psyllium will probably continue to increase. Indian psyllium is already a large-scale export-oriented crop. The questions are whether genetic variability can be preserved and used for maintaining and improving crop quality and yields and whether India will maintain its long-term dominance on psyllium cultivation for the international market. HG

**—Gayle Engels and Josef Brinckmann**

## References


1. Singh N, Lal RK, Shasany AK. Phenotypic and RAPD diversity among 80 germplasm accessions of the medicinal plant isabgol (*Plantago ovata*, Plantaginaceae). *Genet Mol Res.* 2009;8(4):1273-1284.
2. Tutel B, Kandemir I, Kuş S, Kence A. Classification of Turkish *Plantago* L. species using numerical taxonomy. *Turk J Bot.* 2005;29(1):51-61.
3. Applequist W. *The Identification of Medicinal Plants: A Handbook of the Morphology of Botanicals in Commerce*. Austin, TX: American Botanical Council; St. Louis, MO: Missouri Botanical Garden Press; 2006.
4. Dhar MK, Friebe B, Kaul S, Gill BS. Characterization and physical mapping of ribosomal RNA gene families in Plantago. *Ann Bot.* 2006;97(4):541-548.

5. Amanullah, Khetran MA, Badani LA, et al. Comparative study on yield and yield components of psyllium *Plantago ovata* varieties in Balochistan. *J Pharmacogn Phytochem.* 2016;5(6):270-272.
6. Batanouny KH, Aboutabl E, Shabana M, Soliman F. Pharmacopoeial Wild Medicinal Plants in Egypt. In: Batanouny KH, ed. *Wild Medicinal Plants in Egypt: An Inventory to Support Conservation and Sustainable Use*. Cairo, Egypt: Academy of Scientific Research and Technology; Morges, Switzerland: International Union for Conservation; 1999.
7. Ebadi-Almas D, Karimzadeh G, Mirzaghaderi G. Karyotypic variation and karyomorphology in Iranian endemic ecotypes of *Plantago ovata* Forsk. *Cytologia.* 2012;77(2):215-223.
8. Jat RS, Reddy RN, Bansal R, Manivel P. *Good Agricultural Practices for Isabgol.* Anand, Gujarat, India: Dr. Jitendra Kumar, Director, ICAR – Directorate of Medicinal and Aromatic Plants Research; 2015.
9. Meyers SC, Liston A. The biogeography of *Plantago ovata* Forssk. (Plantaginaceae). *Int J Plant Sci.* 2008;169(7):954-962.
10. Brinckmann JA. Short supply and price increases foreseen for 2014 ispaghula crop. *Market Insider for Medicinal Plants & Natural Ingredients*. June 26, 2014. www.intracen.org/itc/blogs/market-insider/Short-supply-and-price-increases-foreseen-for-2014-ispaghula-crop/. Accessed January 28, 2018.
11. Lal RK, Khanuja SPS, Agnihotri AK. Psyllium (*Plantago ovata* F), its Conservation and Utilisation. In: Trivedi PC, ed. *Medicinal Plants Utilisation and Conservation*. 2nd ed. Jaipur, Rajasthan, India: Prem C. Bakliwal, Aavishkar Publishers, Distributors; 2009:120-129.
12. Sarfraz RM, Khan H, Maheen S, et al. *Plantago ovata*: A comprehensive review on cultivation, bio-chemical, pharmaceutical and pharmacological aspects. *Acta Pol Pharm — Drug Res.* 2017;74(3):739-74
13. Li Z, Wei L, Hoggard RK. Plantaginaceae. In: Wu Z, Raven PH, Hong D, eds. *Flora of China*. Vol 19. Beijing, China: Science Press; St. Louis, MO: Missouri Botanical Garden; 2011:495-503.
14. European Pharmacopoeia Commission. *European Pharmacopoeia (PhEur 9.3).* Strasbourg, France: European Directorate for the Quality of Medicines; 2017.
15. United States Pharmacopeial Convention. *United States Pharmacopeia, Fortieth Revision (USP 40).* Rockville, MD: United States Pharmacopeial Convention; 2017.
16. National Multi-Commodity Exchange of India Limited (NMCE). *Report on Isabgul Seed.* Ahmedabad, Gujarat, India: NMCE; 2010.
17. Tournefort JP. *Institutiones rei herbariae, editio altera.* Parisiis (Paris, France): E Typographia Regia; 1700.
18. Linné Cv, Salvius L. *Caroli Linnaei ... Species plantarum :exhibentes plantas rite cognitas, ad genera relatas, cum differentiis specificis, nominibus trivialibus, synonymis selectis, locis natalibus, secundum systema sexuale digestas...* Holmiae (Stockholm, Sweden): Impensis Laurentii Salvii; 1753.
19. Linné CV, Salvius L. *Caroli Linnaei...Systema naturae per regna tria naturae :secundum classes, ordines, genera, species, cum characteribus, differentiis, synonymis, locis.* Holmiae (Stockholm, Sweden): Impensis Direct. Laurentii Salvii; 1759.
20. Brummitt RK. Report of the Nomenclature Committee for Vascular Plants: 60. *Taxon.* 2009;58(1):280-292.
21. Indian Pharmacopoeia Commission. *Indian Pharmacopoeia 2010, Sixth Edition.* Ghaziabad, Uttar Pradesh, India: Indian Pharmacopoeia Commission, Ministry of Health & Family Welfare, Govt. of India; 2010.
22. Directorate of Marketing & Inspection (DMI), Ministry of Agriculture (MoA), Government of India. *Isabgol Husk Grading and Marking Rules, 1982.* Faridabad, Haryana, India: DMI, MoA, Government of India; 1982.
23. National Multi-Commodity Exchange of India Limited (NMCE). *Minutes of the first meeting of the Trade Advisory Committee for Isabgul held on 8th December 2016 at Sidhpur in Hotel Marigold.* Ahmedabad, Gujarat, India: NMCE; 2016.
24. Brinckmann JA. Reproducible efficacy and safety depend on reproducible quality: Matching the various quality standards that have been established for botanical ingredients with their intended uses in cosmetics, dietary supplements, foods, and medicines. *HerbalGram.* 2011(91):40-55.
25. US Food and Drug Administration. Proposal To Establish Monographs for OTC Laxative, Antidiarrheal, Emetic, and Antiemetic Products. *Federal Register.* 1975;40(56):12902-12944.
26. US Food and Drug Administration. Laxative Drug Products for Over-the-Counter Human Use; Tentative Final Monograph. *Federal Register.* 1985;50(10):2124-2158.
27. US Food and Drug Administration. Laxative Drug Products for Over-the-Counter Human Use; Tentative Final Monograph; Notice of Proposed Rulemaking. *Federal Register.* 1986;51(190):35136-35137.
28. US Food and Drug Administration. Laxative Drug Products for Over-The-Counter Human Use; Tentative Final Monograph; Reopening of Administrative Record. *Federal Register.* 1992;57(106):23174-23172.
29. US Food and Drug Administration. Laxative Drug Products for Over-the-Counter Human Use; Psyllium Ingredients in Granular Dosage Forms; Final Rule. *Federal Register.* 2007;72(60):14669-14674.
30. US Food and Drug Administration. Food Labeling: Health Claims; Soluble Fiber From Certain Foods and Coronary Heart Disease; Final Rule. *Federal Register.* 1998;63(32):8103-8121.
31. US Food and Drug Administration. Regulations on Statements Made for Dietary Supplements Concerning the Effect of the Product on the Structure or Function of the Body; Final Rule. *Federal Register.* 2000;65(4):1000-1050.
32. Blumenthal M, Busse WR, Goldberg A, et al., eds. *The Complete German Commission E Monographs Therapeutic Guide to Herbal Medicines.* Austin, TX: American Botanical Council; Boston, MA: Integrative Medicine Communication; 1998.
33. Committee on Herbal Medicinal Products (HMPC). *Community Herbal Monograph on Plantago afra* L. *et Plantago indica* L., *semen.* London, UK: European Medicines Agency; 2013.
34. Committee on Herbal Medicinal Products (HMPC). *Community Herbal Monograph on Plantago ovata Forssk., seminis tegumentum.* London, UK: European Medicines Agency; 2013.
35. Committee on Herbal Medicinal Products (HMPC). *Community Herbal Monograph on Plantago ovata Forssk., semen.* London, UK: European Medicines Agency; 2013.
36. World Health Organization. *WHO Monographs on Selected Medicinal Plants.* Vol 1. Geneva, Switzerland: World Health Organization; 1999.
37. World Health Organization. *WHO Monographs on Selected Medicinal Plants.* Vol 3. Geneva, Switzerland: World Health Organization; 2007.
38. Indian Pharmacopoeia Commission. *National Formulary of India, 4th Edition, 2011.* Ghaziabad, Uttar Pradesh, India: Indian Pharmacopoeia Commission, Government of India, Ministry of Health & Family Welfare; 2011.
39. US Food and Drug Administration. 21 CFR Part 111 Current Good Manufacturing Practice in Manufacturing, Packaging, Labeling, or Holding Operations for Dietary Supplements; Final Rule. *Federal Register.* 2007;72(121):34752-34958.
40. Fischer MH, Yu N, Gray GR, Ralph J, Anderson L, Marlett JA. The gel-forming polysaccharide of psyllium husk (*Plantago ovata* Forsk). *Carbohydr Res.* 2004;339(11):2009-2017.

41. Olson BH, Anderson SM, Becker MP, et al. Psyllium-enriched cereals lower blood total cholesterol and LDL cholesterol, but not HDL cholesterol, in hypercholesterolemic adults: results of a meta-analysis. *J Nutr.* 1997;127(10):1973-1980.
42. Williams PG. The benefits of breakfast cereal consumption: a systematic review of the evidence base. *Adv Nutr.* 2014;5(5):636S-673S.
43. Anderson JW, Allgood LD, Lawrence A, et al. Cholesterol-lowering effects of psyllium intake adjunctive to diet therapy in men and women with hypercholesterolemia: meta-analysis of 8 controlled trials. *Am J Clin Nutr.* 2000;71(2):472-479.
44. Ribas SA, Cunha DB, Sichieri R, Santana da Silva LC. Effects of psyllium on LDL-cholesterol concentrations in Brazilian children and adolescents: a randomised, placebo-controlled, parallel clinical trial. *Br J Nutr.* 2015;113(1):134-141.
45. Yang J, Wang HP, Zhou L, Xu CF. Effect of dietary fiber on constipation: a meta analysis. *World J Gastroenterol.* 2012;18(48):7378-7383.
46. Paré P, Fedorak RN. Systematic review of stimulant and nonstimulant laxatives for the treatment of functional constipation. *Can J Gastroenterol Hepatol.* 2014;28(10):549-557.
47. McRorie JW, Daggy BP, Morel JG, Diersing PS, Miner PB, Robinson M. Psyllium is superior to docusate sodium for treatment of chronic constipation. *Aliment Pharmacol Ther.* 1998;12(5):491-497.
48. Shulman RJ, Hollister EB, Cain K, et al. Psyllium fiber reduces abdominal pain in children with irritable bowel syndrome in a randomized, double-blind trial. *Clin Gastroenterol Hepatol.* 2017;15(5):712-719.
49. Khan K, Jovanovski E, Ho HVT, et al. The effect of viscous soluble fiber on blood pressure: A systematic review and meta-analysis of randomized controlled trials. *Nutr Metab Cardiovasc Dis.* 2018;28(1):3-13.
50. Brum JM, Gibb RD, Peters JC, Mattes RD. Satiety effects of psyllium in healthy volunteers. *Appetite.* 2016;105:27-36.
51. Export Import Data Bank Version 7.1 - TRADESTAT. Kolkata, India: Government of India, Ministry of Commerce & Industry; 2017. http://commerce.gov.in/eidb/default.asp. Accessed October 7, 2017.
52. Global Agricultural Trade System (GATS) Online. Washington, DC: US Department of Agriculture Foreign Agricultural Service; 2017. Available at: https://apps.fas.usda.gov/gats/. Accessed October 7, 2017.
53. Smith T, Kawa K, Eckl V, Morton C, Stredney R. Market Report: Herbal supplement sales in US increase 7.7% in 2016. *HerbalGram.* 2017(115):56-65.
54. About Sarvoday. Sarvoday Sat Isabgol Factory website. Available at: www.sarvodaypsyllium.com/about_us.htm. Accessed January 28, 2018.
55. Allen D, Bilz M, Leaman DJ, Miller RM, Timoshyna A, Window J. *European Red List of Medicinal Plants.* Luxembourg: Publications Office of the European Union; 2014.
56. Kumar M, Fougat RS, Sharma AK, et al. Phenotypic and molecular characterization of selected species of *Plantago* with emphasis on *Plantago ovata*. *Austr J Crop Sci.* 2014;8(12):1639-1647.
57. Fougat R, Joshi C, Kulkarni K, et al. Rapid development of microsatellite markers for *Plantago ovata* Forsk.: Using next generation sequencing and their cross-species transferability. *Agriculture.* 2014;4(2):199-216.
58. Harrison RG, Larson EL. Hybridization, introgression, and the nature of species boundaries. *J Hered.* 2014;105(S1):795-809.
59. Karimi D, Heidari B, Daneshnia SN, Dadkhodaie A. Genetic variation and interrelationship of seed mucilage, swelling factor and agronomic traits in *Plantago ovata* wild accessions. *Ann Biol Res.* 2013;4(5):175-182.

**Psyllium** *Plantago afra* in Kavo Ckreko, Cyprus
Photo ©2018 Krzysztof Ziarnek

# ADOPT-AN-HERB

## HerbMedPro™ PROGRAM

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

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

HerbMedPro provides online access to abstracts of scientific and clinical publications on more than 250 commonly used medicinal herbs. A free version, HerbMed®, is available to the general public. HerbMed features 20 to 30 herbs from HerbMedPro that are rotated on a regular basis with an emphasis on 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.

## Herbal Adopters

| | |
|---|---|
| Natural Factors | **Echinacea** *Echinacea* spp. |
| Nature's Gift | **Helichrysum** *Helichrysum italicum* |
| PharmActive Biotech Products | **Saffron** *Crocus sativus* |
| Nature's Sunshine | **Cayenne** *Capsicum annuum* |
| 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 LLC | **Baobab** *Adansonia digitata* |
| | **Rooibos** *Aspalathus linearis* |
| Beehive Botanicals | **Propolis** |
| Natural Health International Conscious \| Leading \| Empowering | **Maca** *Lepidium meyenii* |
| Verdure Sciences® | **Pomegranate** *Punica granatum* |
| Artemis International | **Purple Corn** *Zea mays* |
| utzy naturals | **Black Chokeberry** *Aronia melanocarpa* |
| | **Elderberry** *Sambucus nigra* |
| | **Stinging Nettle** *Urtica dioica* |
| Four Elements | **Lemon Balm** *Melissa officinalis* |
| afrigetics BOTANICALS | **Bulbine** *Bulbine natalensis* |
| Brassica Protection Products | **Broccoli** *Brassica oleracea* Broccoli Group |
| indena® | **Indian Frankincense** *Boswellia serrata* |
| DownUnder enterprises | **Tea Tree** *Melaleuca alternifolia* |
| Aromatics International | **Peppermint** *Mentha x piperita* |
| HERBALIFE® | **Aloe Vera** *Aloe vera* |

# Adoptions by Beehive Botanicals and Embria Health Sciences Support ABC's Adopt-an-Herb Program

**The American Botanical Council (ABC) welcomes Beehive Botanicals' adoption of propolis and Embria Health Sciences' adoption of EpiCor fermentate through ABC's Adopt-an-Herb botanical education program. Propolis is a natural, plant-derived bee product that has been used medicinally by humans for centuries, and EpiCor fermentate is a whole-food fermentation ingredient that supports the immune and digestive systems.**

These adoptions support ABC's extensive HerbMedPro database, ensuring that this essential educational resource remains up to date for researchers, health professionals, industry, students, consumers, and members of the herbal and dietary supplements community. HerbMedPro is a comprehensive, interactive online database that provides access to important scientific and clinical research data on the uses and health effects of more than 250 herbs, spices, medicinal plants, and related substances.

ADOPT-AN-HERB
HerbMedPro™ PROGRAM

BEEHIVE BOTANICALS® **Propolis**

## Propolis Adoption

"Beehive Botanicals is committed to quality, purity, and integrity," wrote Michelle Forrester, the company's chief financial officer, adding that participation in the Adopt-an-Herb program reflects the company's commitment to integrity by providing unbiased information on the benefits of propolis.

ABC Founder and Executive Director Mark Blumenthal said: "We are deeply grateful for Beehive Botanicals' adoption of propolis on ABC's HerbMedPro website. As a former beekeeper, I personally appreciate the opportunity for ABC to create an HerbMedPro record on the scientific and clinical research on this fascinating healing substance."

## About Propolis

Propolis, or bee glue, is a complex, sticky, resinous, wax-like mixture that is produced by some bee species, including the Western, or European, honeybee (*Apis mellifera*, which is managed widely by beekeepers) and some stingless bees (meliponines). To make propolis, these bees collect plant secretions (lipophilic materials on leaves and leaf buds, mucilages, gums, resins, latexes, etc.) and often mix them with beeswax and saliva and sometimes other substances, such as honey. Some meliponines are known to also sometimes mix in earth (clay, mud, etc.) when making propolis, but *A. mellifera* reportedly is not known to do this.

The bees may cut plant tissues to release the exudate used to make propolis and may also collect material exuded from preexisting wounds in plants. The chemical composition of propolis can vary significantly and depends mainly on the plant species near the hive, but also on the season, altitude, illumination, collecting bee species, and other factors. Propolis consists mainly of plant resins and beeswax and contains essential oils, phenolic compounds, and pollen.

Propolis reportedly is derived mostly from plant species in the North Temperate Zone (which extends from the Tropic of Cancer to the Arctic Circle), including species of alder (*Alnus* spp., Betulaceae), beech (*Fagus* spp., Fagaceae), birch (*Betula* spp., Betulaceae), elm (*Ulmus* spp., Ulmaceae), poplar (*Populus* spp., Salicaceae), willow (*Salix* spp., Salicaceae), and conifers such as pine (*Pinus* spp., Pinaceae). The color of propolis can vary from green to brown and reddish, depending on the botanical source(s).

The word "propolis" derives from the Greek *pro*, meaning "in front of" or "at the entrance to," and *polis*, meaning "community" or "city," presumably because bees use it to defend the hive. Specifically, they use it as cement to seal cracks and reinforce the structural stability of the hive and to make the entrance of the hive weathertight and easier to defend. They also apply it to areas where combs are to be attached, which creates smooth and germ-free surfaces. In addition, they use it to embalm hive invaders that have died, if they are not able to remove the carcass from the hive. Propolis is reportedly responsible for the lower incidence of microorganisms inside the hive than outside and helps prevent infection of larvae, honey stores, and combs.

There is evidence that the ancient Egyptians, Persians, and Romans all used propolis. In the first century, the Greek physician Dioscorides and the Roman naturalist Pliny the Elder wrote about its benefits. Traditionally, propolis has been used internally and externally to treat wounds, burns, ulcers, rheumatism, myalgia, eczema, and cough, and to draw out thorns and splinters. Propolis has demonstrated anesthetic, antibacterial, antifungal, anti-inflammatory, antioxidant, antiviral (including anti-herpes and anti-HIV), cytotoxic, and immunomodulatory properties. It has been used in food and beverages for its health benefits.

## About Beehive Botanicals

Hayward, Wisconsin-based Beehive Botanicals was established in 1972 by Warren Ogren and began by exporting only one product, propolis, to Europe. It was many years

before consumers in the United States became interested in propolis, according to the company. Although propolis remains an important part of the company's business, consumers eventually asked for a broader selection of products, and Beehive Botanicals now offers bee pollen, royal jelly, and unique items such as throat sprays, extracts, and tinctures with propolis, as well as propolis lip balm. Beehive Botanicals also provides contract manufacturing of dietary supplements, along with raw material and bulk encapsulation, powder, and liquid filling.

The company, which is the largest dealer of propolis in North America according to its website, is committed to maintaining NSF International certification to ensure that its manufacturing process adheres to high-quality standards. The company also values philanthropy and contributes regularly to local food shelters, the local school district and humane society, and other causes.

Beehive Botanicals sources propolis from the United States, China, and Brazil and standardizes its propolis based on the flavonoids pinocembrin, chrysin, galangin, and quercetin. The standardization process involves alcohol extraction and removal of wax.


## EpiCor Fermentate Adoption

"As a science-based ingredient manufacturer, Embria is proud to have EpiCor fermentate be a part of the Adopt-an-Herb Program," said Jeff Cannon, CEO of Diamond V, Embria's parent company. "EpiCor, a unique immune and digestive support ingredient with years of human clinical research, brings a novel ingredient category to the HerbMedPro database. This partnership will help provide ABC's audience of researchers and educators access to a wealth of vital research for addressing immune and gastrointestinal challenges."

Blumenthal thanked Embria Health Sciences for its much-appreciated support of ABC's nonprofit educational efforts and expressed his enthusiasm for the addition of a new ingredient to the database. "EpiCor has a unique story of discovery," he said. "When Embria executives realized that workers who were exposed to the yeast in the company's manufacturing facility made fewer claims for health care benefits than office workers in another building, this led to the research and development of what became EpiCor: a unique example of a real-world observation that resulted in the creation of a new natural health-promoting ingredient."

## About EpiCor

EpiCor is a safe and natural whole-food fermentation ingredient that supports the immune and digestive systems. It combines heat-inactivated baker's yeast (*Saccharomyces cerevisiae*, Saccharomycetaceae) and the fermentation broth that was used for its growth, yielding a complex, nutrient-rich ingredient composed of immune-supporting metabolites as well as proteins, vitamins, minerals, amino acids, polyphenols, and beta glucans. Made through a proprietary fermentation process, EpiCor is different from synthesized commodities such as nutritional yeast or isolated beta-glucan ingredients. More than 10 studies on EpiCor have been published, including seven human clinical trials and multiple safety studies.

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

## About Embria Health Sciences

Embria Health Sciences is dedicated to creating and manufacturing natural, science-based ingredients that support wellness and vitality. Embria offers consistent and reliable ingredients by having dedicated professionals use leading-edge technology in manufacturing and quality systems, made in America and supported by extensive research.

## About Adopt-an-Herb and HerbMedPro

Beehive Botanicals and Embria Health Sciences are two of 50 companies that have supported ABC's educational efforts to collect, organize, and disseminate reliable, traditional, and science-based information, including clinical studies, on herbs, medicinal plants, and other botanical- and fungal-based ingredients through the Adopt-an-Herb Program. This program encourages companies, organizations, and individuals to "adopt" one or more specific herbs for inclusion and ongoing maintenance in the HerbMedPro database. To date, 56 herbs have been adopted.

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

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

**—ABC Staff**

# American Botanical Council Welcomes Three New Board of Trustees Members

**In December 2017, the American Botanical Council (ABC) announced the election of three new members to its Board of Trustees: Bethany Davis; Richard Kingston, PharmD; and Holly Shimizu. The new trustees bring decades of combined experience in a diverse range of fields related to medicinal plants. Davis, Kingston, and Shimizu are recognized leaders in dietary supplement industry regulation and environmental sustainability practices; clinical toxicology, botanical safety, and pharmacy; and public horticulture and herbal education, respectively.**

"ABC is delighted to welcome Bethany, Holly, and Rick to our Board of Trustees," said ABC Founder and Executive Director Mark Blumenthal. "Each of these new board members has numerous skills and strengths that will help ABC achieve new successes in the fields of medicinal plant education and research. Now that ABC is in its 30th year, and as ABC determines its future growth and direction, these new trustees will help empower the board and ABC to fulfill its unique nonprofit educational mission, publications, and programs."

The addition of these three experts brings the total number of ABC Board of Trustees members to 11. In April 2017, longtime ABC trustee Fredi Kronenberg, PhD, a champion of integrative medicine for women's health, died after a long illness. The decision to expand the board was made unanimously at the annual Board of Trustees meeting at ABC's headquarters in November 2017. More information about the eight other board members can be found on ABC's website.

## Bethany Davis

Since 2011, Davis has worked for FoodState, a whole-food supplements company based in Manchester, New Hampshire, which owns two well-known supplement brands: MegaFood and INNATE Response Formulas. Currently, she is the company's director of regulatory and industry affairs.

"I am so honored to be serving on the ABC Board of Trustees," Davis said. "ABC's legacy and authority is widely known around the world. I am excited to participate on the ABC board and serve the global herbal community."

Before joining FoodState, Davis worked as the chain pharmacy account manager for Adheris Health, a provider of direct-to-patient medication adherence programs, and as the owner-operator of Davis Health Consulting, a regulatory consulting firm. She has a master's degree in regulatory affairs and health policy from the Massachusetts College of Pharmacy and Health Sciences in Boston, Massachusetts.

Davis's passion for health care, coupled with her experience in the pharmaceutical industry and background in health policy and regulation, eventually led her to the natural products industry. "Through earning my Master of Science in regulatory affairs and health policy, the grave state of health care in the United States was made clear to me," she said. "The value of traditional herbal therapies and the potential for positive impact on human health through dietary supplementation is of the utmost importance."

Davis is actively involved in promoting sustainability, transparency, and non-genetically modified organism (GMO) issues related to the natural products industry.

"I have dedicated my professional life to growing the dietary supplement industry, bringing together educators, experts, and collaborators of all types in order to serve the public health," she said. "As a mother and a birth worker, and as a strong, lifelong advocate of personal empowerment, ABC's mission of bringing forth science-based education to promote the responsible use of herbal medicine resonates strongly. Everyone should be able to use herbs safely and with proper knowledge and access to take control of their health. A noble cause, and one I aim to serve wholeheartedly."

In addition to her current position with FoodState, Davis is the president of the Coalition for Supplement Sustainability, a group of supplement and ingredient companies dedicated to promoting non-GMO and sustainable supply chains. She is also a voting board member of the Massachusetts General Hospital Partners Institutional Review Board and a member of the American Herbal Products Association's Board of Trustees.

## Richard Kingston, PharmD

Kingston is the co-founder and president of regulatory and scientific affairs at SafetyCall International, a company that specializes in adverse event management and regulatory compliance services, where he has worked since 2004. He is also a longtime faculty member at the University of Minnesota (UM), where he has worked for more than 35 years and currently is a clinical professor of pharmacy. At UM, he is the course director for "Therapeutics of Herbs and Other Natural Medicinals," which is taught in the College of Pharmacy and available to all students in the Academic Health Center. In addition, Kingston has been an adjunct professor at the

National Center for Natural Products Research (NCNPR), an FDA Center of Excellence at the University of Mississippi College of Pharmacy, since 2014.

"I'm honored and grateful for the opportunity to serve on the ABC Board of Trustees," said Kingston, who has been on the ABC Advisory Board since 2002. "ABC has an exemplary reputation for its work in providing all stakeholders with science-based information to promote the safe and responsible use of herbs and medicinal plants.

"I'm particularly interested in helping ABC further its efforts with the Botanical Adulterants Prevention Program, and I commend ABC for taking a leadership role in bringing the global herb industry together to address this critical issue," Kingston continued. "The integrity of the botanical supply chain ensures the safety of consumers, and that remains an important part of my efforts and focus in my work. In my new capacity as a member of the distinguished ABC Board of Trustees, I look forward to contributing to a number of areas related to botanical safety, while also being committed to the organization's overall future success."

Kingston received his doctor of pharmacy degree from the University of Minnesota College of Pharmacy. He completed his postdoctoral fellowship in clinical toxicology and pharmacokinetics in the Section of Clinical Pharmacology and the Clinical Toxicology Treatment Program at the University of Minnesota-affiliated level 1 trauma center, St. Paul-Ramsey Medical Center. After his postdoctoral training, he was the co-founder and managing director of the Minnesota Poison Control system and the Minnesota Regional Poison Center. He has also served as a faculty member for the Graduate Minor Program in Complementary Therapies and Healing Practices at the Center for Spirituality and Healing at the University of Minnesota Academic Health Center.

Kingston is a member of numerous professional organizations, including the American Association of Poison Control Centers, the American Academy of Clinical Toxicology, the Household and Commercial Products Association, and the Society of Toxicology, among others.

Throughout his career, Kingston has given more than 200 lectures and presentations, and has authored or co-authored more than two dozen articles in various publications and scientific journals, including the *Annals of Internal Medicine*, *American Journal of Pharmaceutical Education*, and *Veterinary and Human Toxicology*. He has also contributed to five textbooks, including serving as a co-editor of *Herbal Products: Toxicology and Clinical Pharmacology* (Humana Press, 2007) and as the author of a chapter on herbal, traditional, and alternative medicines in *Clinical Management of Poisoning and Drug Overdose*, 4th edition (Elsevier Press, 2007).

### Holly Shimizu

Shimizu has held numerous leadership positions in the fields of public horticulture, herbal education, and plant conservation. From 2000 to 2014, she served as the executive director of the United States Botanic Garden (USBG), one of the oldest botanical gardens in the United States, which is located on the National Mall in front of the US Capitol Building in Washington, DC.

"Becoming actively involved with the American Botanical Council as a member

of the Board of Trustees is very exciting to me because the work of ABC is so important," said Shimizu, who has served on the ABC Advisory Board since 2006. "So many of us count on this work as our trusted, reliable source for information that is current and scientifically accurate."

During her time as executive director of the USBG, Shimizu led the effort for the garden to become a founding partner of the Sustainable Sites Initiative, which is considered one of the most comprehensive certification systems for sustainable land management and development. Before becoming executive director, Shimizu was the USBG's assistant executive director and public programs manager.

Shimizu has also served as an advisor for the White House gardens and played a role in redesigning the Rose Garden in 1983. She also worked with former first lady Laura Bush on a long-term botanical research and identification project for Camp David.

Most recently, Shimizu was the interim executive director of the American Horticultural Society in Alexandria, Virginia. She has also served as the managing director of the Lewis Ginter Botanical Garden in Richmond, Virginia, and was the first curator of the National Herb Garden at the US National Arboretum in Washington, DC. Shimizu received a master's degree in horticulture from the University of Maryland.

"In my work with plants over the years, I have focused on the importance of plants to our health and well-being, their chemistry, complexity, beauty, and conservation," Shimizu said. "For plants to receive their rightful place in our universe, we need to encourage people to respect the extraordinary role plants play in human and animal lives, as well as in the natural world. I have always been driven to find various ways for people to grasp a greater understanding of plants, to actually 'see' them, and to integrate them into American culture."

Shimizu is currently on the board of directors of numerous organizations, including the American Horticultural Society and Friends of the National Arboretum, and is on the advisory boards of the Southern Delaware Botanic Gardens and the Las Cruces Biological Station/Wilson Botanical Garden in Costa Rica, which is part of the nonprofit Organization for Tropical Studies. Previously, she served on the boards of the American Public Gardens Association and Botanic Gardens Conservation International, as the chair of botany and horticulture for the Herb Society of America, and on the advisory council for Longwood Gardens.

"Exploring the plants around us, learning about their uses, their value in various cultures, is an expansive and never-ending pursuit," Shimizu added. "ABC helps us to unravel some of the plant mysteries, while also providing much-needed practical information on botanical adulterants and product quality, and dependable sources for materials and further information. I am delighted to be a part of these efforts in working with the American Botanical Council."

Throughout her career, Shimizu has received many recognitions and honors, including an honorary doctorate from Washington College in Chestertown, Maryland, the Thomas Roland Medal for Outstanding Contributions to Horticultural Education from the Massachusetts Horticultural Society, the Professional Award for an Outstanding Public Garden Director from the American Horticultural Society, and the Nancy Putnam Howard Award from the Herb Society of America.

Shimizu has contributed articles to a variety of publications, including *The New York Times*, *Horticulture*, and *Fine Gardening*, among others. Most recently, she co-authored a chapter in *Living in the Anthropocene: Earth in the Age of Humans* (Smithsonian Institution, 2017). HG

**—ABC Staff**

# American Botanical Council Publishes 7,000th HerbClip Research Summary

**In mid-January, the American Botanical Council (ABC) published its 7,000th HerbClip. An essential research and educational resource for scientists, researchers, health professionals, industry members, and others, HerbClips are two- to three-page summaries and critical reviews of scientific journal articles that cover medicinal plant-related human clinical research, analytical methods, regulatory data, market information, ethnobotanical reviews, conservation and sustainability studies, and more.**

ABC members at the Academic level and above can access the entire HerbClip database containing the 7,000-plus summaries. ABC Sponsor Members and HerbClip Service Members also receive HerbClips and, when available, the PDF versions of the original articles on which they are based.

HerbClip summaries typically focus on the growing body of human clinical trials on herbs and phytomedicinal products, including systematic reviews and meta-analyses. HerbClips are based on articles from a wide variety of peer-reviewed scientific and medical journals, as well as monographs, government documents, special reports, trade journals, and news articles. In addition to summarizing the original article, HerbClips often include insights, perspectives, criticism, and links to other relevant articles or resources.

When applicable, HerbClip reviews provide the trade name of the medicinal product on which a clinical study is based (including the name of the company that produced the product), as well as a description of the tested material. To help ensure accuracy, HerbClip summaries and reviews are vetted by editors and peer reviewers before they are published.

HerbClip started in 1992, four years after ABC was founded. At the time, ABC Founder and Executive Director Mark Blumenthal would photocopy relevant news and scientific articles and mail them to friends and colleagues. About a year later, when he learned that this activity had become increasingly costly, Blumenthal called two friends in the herb industry — Jim Beck, founder and then-owner of Solaray, and Ken Murdock, then-president and owner of Nature's Way — and asked if they would be willing to pay for summaries of the latest herb research and related developments. They agreed, as did many others over a short period of time, and HerbClip became a permanent, funded ABC publication.

HerbClip initially involved mailing summaries and reviews of herbal literature to ABC colleagues in the academic and scientific communities, as well as members of industry. As far as is known, no similar service existed in the herb and natural medicine community and herbal supplement industry at the time. In 2005, ABC added "HerbClip News" (a column of commentary from HerbClip Managing Editor Lori Glenn) with each mailing. Two years later, in 2007, the first electronic HerbClips were sent to ABC members, which dramatically expanded readership. By 2009, all HerbClips were delivered electronically, reflecting ABC's commitment to environmental sustainability.


"ABC is profoundly grateful to Lori Glenn, the HerbClip managing editor for these past 15 years, as well as Heather Oliff, PhD, Mariann Garner-Wizard, and Shari Henson — all of whom have been writing HerbClips for more than a decade — and all of the other HerbClip writers, editors, and peer reviewers who have contributed to creating this unique and useful research and educational resource," said Blumenthal. "Along with ABC's quarterly, peer-reviewed journal *HerbalGram*, HerbClip stands out as one of ABC's most unique and valuable educational publications. In all the world's phytomedicinal literature, there is nothing like HerbClip."

Stefan Gafner, PhD, chief science officer of ABC and technical director of the ABC-AHP-NCNPR Botanical Adulterants Prevention Program wrote: "In my work, performing a literature search on a botanical ingredient or reading a clinical study in its full length is often done only when needed for a specific project. Therefore, to continue being informed on important new studies is a challenging task. With its short and easily understandable summaries, HerbClip gives me the opportunity to stay on top of pertinent data on the efficacy and safety of herbal medicines without an extensive investment of time and energy."

Glenn wrote: "As an educational tool, HerbClip provides concise, easy-to-use information to busy professionals and the general public." She added that the database of more than 7,000 HerbClips exposes professionals to topics that may not be a part of their normal research or study areas. In addition, HerbClip is a resource that educators can share with students and that herb ingredient and product suppliers and natural food stores can share with customers.

"As the HerbClip managing editor, I have been blessed to work with many amazing writers, consulting editors, peer reviewers, and ABC staff members, who have been a part of the HerbClip process," Glenn added. "I am deeply grateful for the time and energy they have dedicated to making HerbClip a beneficial educational program."

Oliff, of California-based Science Consulting Group, LLC, wrote: "This is a momentous milestone, and I am honored to think that I have been an important part of reaching this milestone. I have been writing HerbClips monthly for 18 years (and counting), and have written nearly 20% of the 7,000 HerbClips! One of the best things about the HerbClip service is that it includes summaries of many articles that would be difficult or costly to obtain otherwise. Also, I appreciate that the HerbClips are peer reviewed, which ensures accuracy and that the HerbClip product exceeds standards of excellence."

In a 1992 letter to Blumenthal, renowned ethnobotanist and ABC co-founder James A. Duke, PhD, who passed away on December 10, 2017, praised the then-new HerbClips he received while still working at the Agricultural Research Service at the United States Department of Agriculture. "It's time I thanked you for your new HerbClip service you've been sending lately," Duke wrote. "I'm always happy to see them…. Truly, I look forward to the clippings almost as much as I do the drafts of a new *HerbalGram*. I share your eagerness to know what's new! Your clippings help us very much in that regard."

HerbClip summaries and reviews are available online through the ABC website at www.herbalgram.org. The entire database of more than 7,000 articles is searchable by common and Latin names of herbs, author names, journal and article titles, pharmacological actions, clinical endpoints, conditions, and more. Fifteen new HerbClips and an HerbClip News article are produced twice monthly. At least four HerbClips from each installment are available to the public for free. HG

**—ABC Staff**

# New ABC Employee Profile: Tanya Garduño

**Tanya Garduño joined the American Botanical Council (ABC) staff in December 2016 as the new communications and marketing coordinator. Garduño has many years of experience working in the nonprofit sector, which gives her unique insight into ABC's marketing and member engagement needs.**

Originally from San Antonio, Texas, Garduño moved to Austin, Texas, in 2014 and lives with her husband and two bull terriers. In addition to her full-time work at ABC, Garduño is a part-time student working toward a computer science degree with minors in philosophy and political science. At ABC, Garduño works closely with Development Director Denise Meikel to develop and execute the nonprofit's marketing plan, and assists with development strategies and objectives. She also coordinates communications sent out to the media and ABC members, including member advisories, press releases, fundraising initiatives, and the weekly newsletter Herbal News and Events (HNE). HNE keeps ABC website subscribers up to date with relevant news articles, events in the natural products and herbal medicine communities, and ABC initiatives such as the Adopt-an-Herb Program and HerbClip summaries.

However, Garduño's biggest project for the organization will use her considerable web design skills to modernize and update the ABC website. "I'm really excited about the redesign of the ABC website," Garduño said. "I hope that it will help our members and the public easily navigate and access the important work and research our organization does." According to Garduño, the work on the website is "a chance to make it more user-friendly for visitors, who are frequently accessing it on tablets and cellphones, not just on a computer screen."

Meikel added: "Tanya's nonprofit experience and genuine passion for technology are helping ABC move to the next level in communicating with our members and supporters around the world. It's an exciting time at ABC, and Tanya is playing a key role in that evolution."

Previously, Garduño worked for nonprofits focused on politics, including political action committees and local campaigns in Texas, aiding progressive candidates in elections to various levels of office. Her work also focused on voter education, increasing voter registration, "get out the vote" initiatives, and redistricting efforts.

In her personal life, Garduño likes to stay active. "I enjoy hiking and visiting the beautiful natural areas in and around Austin," she said. "In my spare time, I love to take my dogs and experience the great outdoors."

ABC Founder and Executive Director Mark Blumenthal said: "Tanya brings so much to the table for the organization, including direct engagement and passion for what she does. We're all very pleased to include Tanya as part of the family of ABC staff."

Though Garduño had little background in herbal medicine before arriving at ABC, she is eager to learn more about modalities of natural healing from her ABC colleagues in the beautiful setting of ABC's 2.5-acre Case Mill Homestead. "I really enjoy the support and sense of community at ABC," she said. "The staff really cares about each other and for the mission of the organization." HG

**—Hannah Bauman**

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# Botanical Adulterants Program Changes Name

## *New name incorporates 'Prevention' to emphasize goal and purpose*

**In January, the ABC-AHP-NCNPR Botanical Adulterants Program officially changed its name to the ABC-AHP-NCNPR Botanical Adulterants Prevention Program. The American Botanical Council (ABC) and its partners at the American Herbal Pharmacopoeia (AHP) and the National Center for Natural Products Research (NCNPR) at the University of Mississippi decided to add "Prevention" to the name in order to emphasize the purpose and intent of the program.**

Initiated in 2010, with its first publications released in 2011, the ABC-AHP-NCNPR Botanical Adulterants Prevention Program (with its new acronym BAPP) has dedicated itself to helping prevent industry use of adulterated raw materials, botanical extracts, and essential oils. This is achieved via the publication of credible and authoritative peer-reviewed documents, interviews with trade media, speeches at industry and professional conferences, and direct consultation with members of the industry.

"The program's goal has always focused on prevention," said Mark Blumenthal, founder and executive director of ABC and founder and director of BAPP. "What we've been trying to do is alert industry members about specific botanical materials that we have confirmed as being adulterated, and counsel industry on the optimum laboratory analytical methods to help determine authenticity of botanical ingredients. By adding the word 'Prevention' to the name, we are making our intention clearer to all stakeholders."

Stefan Gafner, PhD, chief science officer of ABC and technical director of BAPP, said: "The name 'ABC-AHP-NCNPR Botanical Adulterants Prevention Program' more accurately reflects the overarching goal of the program. Our initiative strives to give members of the herb and dietary supplement industries the necessary tools to avoid being duped by suppliers of ingredients that have been acciden-

tally or purposefully adulterated, so that products on the market are authentic and provide the benefits that consumers expect.

"In short," Gafner continued, "we try to prevent adulterated products from reaching the shelves. This is mainly done through dissemination of information about known cases of adulteration and by reviewing analytical test methods to promote the optimal laboratory analytical testing practices for the industry."

Roy Upton, director of AHP, said: "The addition of 'Prevention' to our program's name gets to the heart of what it is we hope to achieve in doing this work — prevent adulteration from happening both by shining a light on what is happening in the marketplace and by providing the tools needed for companies and quality control personnel to know exactly what to look for."

### About the ABC-AHP-NCNPR Botanical Adulterants Prevention Program

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

To date, the program has published 37 extensively peer-reviewed articles, Botanical Adulterants Bulletins, Laboratory Guidance Documents, and Botanical Adulterants Monitor e-newsletters. All of the program's publications are freely available on the program's website. HG

**—ABC Staff**

# ABC-AHP-NCNPR Botanical Adulterants Prevention Program Publishes Cranberry and Ginkgo Leaf Extract Adulteration Bulletins

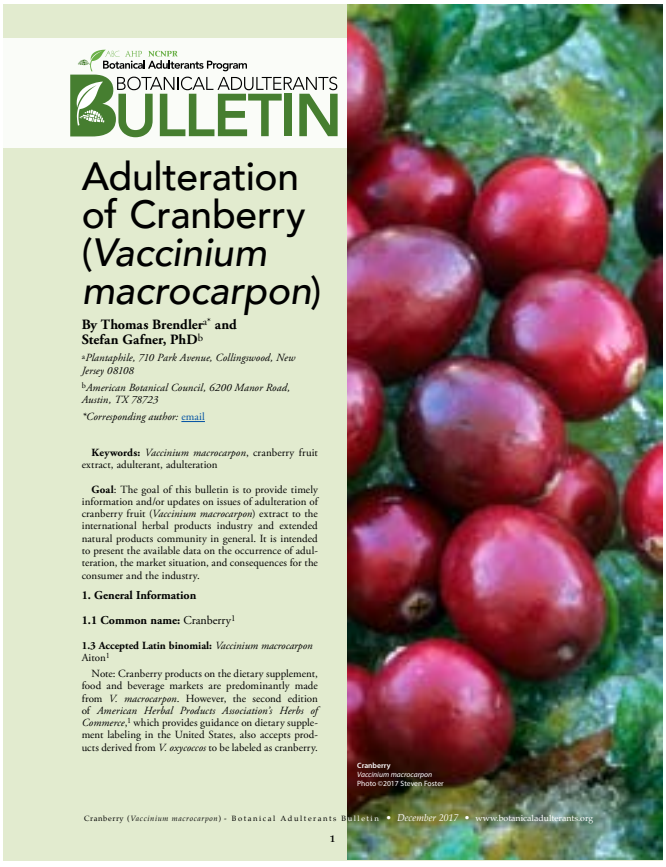
**The ABC-AHP-NCNPR Botanical Adulterants Prevention Program (BAPP) has published two new Botanical Adulterants Bulletins on cranberry (*Vaccinium macrocarpon*, Ericaceae) fruit and ginkgo (*Ginkgo biloba*, Ginkgoaceae) leaf extract. The cranberry and ginkgo bulletins are the 12th and 13th publications, respectively, in the program's series of bulletins.**

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

## Cranberry Bulletin Describes Adulteration with Anthocyanin- or Proanthocyanidin-rich Extracts of Other Plant Species

Cranberry dietary supplements are used widely for the prevention and adjuvant treatment of recurrent urinary tract infections. Cranberry was the second top-selling botanical dietary supplement ingredient in US mainstream retail outlets in 2016, with an 11.9% increase in sales from the previous year.

There are important differences in the composition of the various cranberry supplements on the market, particularly with regard to the content of proanthocyanidins (PACs), which are the cranberry compounds primarily responsible for preventing bacterial adhesion in the urinary tract. The dried press cake, which is the solid material obtained after the fruit juice has been squeezed out, contains approximately 0.8% to 1.5% PACs. The dried press cake makes up more than 50% of the cranberry dietary ingredient supply (i.e., the material sold in bulk for processing into finished cranberry supplements). Other important cranberry ingredients are pure cranberry juice extracts (containing 12% to 24% PACs), whole cranberry fruit extracts (3% to 5% PACs), and blends of cranberry juice extracts with cranberry fruit extracts (3% to 5% PACs). Ingredients with higher concentrations of PACs are more expensive.


ABC-AHP-NCNPR
Botanical Adulterants Program
BOTANICAL ADULTERANTS BULLETIN

Adulteration of Cranberry (*Vaccinium macrocarpon*)

By Thomas Brendler[a,*] and Stefan Gafner, PhD[b]

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**Corresponding author:* email

**Keywords:** *Vaccinium macrocarpon*, cranberry fruit extract, adulterant, adulteration

**Goal**: The goal of this bulletin is to provide timely information and/or updates on issues of adulteration of cranberry fruit (*Vaccinium macrocarpon*) extract to the international herbal products industry and extended natural products community in general. It is intended to present the available data on the occurrence of adulteration, the market situation, and consequences for the consumer and the industry.

**1. General Information**

**1.1 Common name:** Cranberry[1]

**1.3 Accepted Latin binomial:** *Vaccinium macrocarpon* Aiton[1]

Note: Cranberry products on the dietary supplement, food and beverage markets are predominantly made from *V. macrocarpon*. However, the second edition of *American Herbal Products Association's Herbs of Commerce*,[1] which provides guidance on dietary supplement labeling in the United States, also accepts products derived from *V. oxycoccos* to be labeled as cranberry.

Cranberry (*Vaccinium macrocarpon*) - Botanical Adulterants Bulletin • December 2017 • www.botanicaladulterants.org

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Cranberry
*Vaccinium macrocarpon*
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The availability of lower-cost PACs from other plant sources, such as peanut (*Arachis hypogaea*, Fabaceae) skin or grape (*Vitis vinifera*, Vitaceae) seed, has led some suppliers to dilute or replace cranberry PACs — without labeling such dilution or replacement — for financial gain. Other adulterants include anthocyanin-rich extracts from other lower-cost ingredients, such as mulberry (*Morus* spp., Moraceae) fruit, hibiscus (*Hibiscus sabdariffa*, Malvaceae) calyx, black bean (*Phaseolus vulgaris*, Fabaceae) skin, or black rice (*Oryza sativa*, Poaceae). Anthocyanins range in color from red to blue, and anthocyanin-rich extracts are used to mimic the red color found in authentic cranberry extracts.

The new bulletin, written by ethnobotanist and herb industry consultant Thomas Brendler and American Botanical Council (ABC) Chief Science Officer and BAPP Technical Director Stefan Gafner, PhD, provides information about the supply source, production, and market importance of cranberry and its extracts. It also lists the known adulterants, potential therapeutic and/or safety concerns associated with the adulterated ingredients, and laboratory analytical approaches to detect adulterants. Twenty-one expert peer reviewers from academia and industry provided input on the cranberry bulletin.

Gafner explained: "The fact that cranberry extracts are relatively expensive and that lower-cost PACs from other sources are available make them an obvious target for economically motivated adulteration."

He also noted that "some of the commonly used laboratory analytical methods like HPTLC [high-performance thin-layer chromatography] or HPLC-UV [high-performance liquid chromatography with ultraviolet detection] may be fooled by the addition of extraneous PACs. Therefore, adulteration may go undetected unless more sophisticated instrumentation is used, such as MS [mass spectrometry] fingerprinting or HPLC-MS."

Mark Blumenthal, ABC founder and executive director and BAPP founder and director, said: "Cranberry is one of the most popular herbal dietary supplements in the US market, and is used by millions of consumers to help maintain urinary tract health. By publishing this bulletin on the adulteration of cranberry, it is our hope that more supplement manufacturers will be alerted to the unfortunate practices of some unscrupulous ingredient suppliers, thereby not only helping to ensure that manufacturers purchase properly authenticated cranberry ingredients, but also to help ensure that consumers are able to purchase authentic, reliable cranberry supplements."

## Ginkgo Bulletin Details Adulteration with Flavonoids and Flavonoid-rich Extracts from Other Botanical Sources

Ginkgo is one of the most important medicinal plants worldwide. The leaf extracts are used mainly to improve mental performance, for circulatory issues such as peripheral arterial occlusive disease, and for vertigo and tinnitus. Ginkgo leaf extract dietary supplements have been consistently among the 25 top-selling herbal supplements in mainstream and natural retail channels in the United States for more than a decade.

Reports of ginkgo extract adulteration date back to at least 2003, when researchers observed uncharacteristically high amounts of the flavonoid rutin in a sample of bulk material. Numerous subsequent papers have confirmed the addition of flavonoids from extraneous sources, which brings these "ginkgo" extracts into compliance with the 24% flavonol glycoside content standardization required by various pharmacopeial standards. The ginkgo bulletin is the second publication by the program on ginkgo adulteration. In 2016, the BAPP published a review in *HerbalGram* of 11 laboratory analytical studies that documented ginkgo extract adulteration.

The new bulletin, written by Gafner, lists known adulterants, details analytical approaches to detect adulterants, and provides information on the cultivation, harvest, and market importance of ginkgo. The ginkgo extract bulletin was peer-reviewed by 20 experts from academia and industry.

"Ginkgo leaf extract is one of the world's most heavily researched phytomedicines," said Blumenthal. **"**Millions of consumers use ginkgo extracts for a range of health reasons based on frequently positive outcomes from published clinical trials. However, the ginkgo products they are buying, if adulterated, may not perform as well as those ginkgo extracts shown effective in the clinical research. As in many cases of adulteration and fraud, this is a disservice to the public."

Gafner commented: "Adulteration appears to be frequent, with some researchers reporting that more than 70% of the tested samples do not contain authentic ginkgo leaf extract. In some instances, the ginkgo extract is entirely substituted with a flavonol-rich extract, such as a Japanese pagoda tree [*Styphnolobium japonicum*, Fabaceae] flower extract. More often, though, pure flavonols or flavonol-rich extracts are mixed with ginkgo extracts to produce, or attempt to produce, a constituent profile that complies with many pharmacopeial standards of 24% flavonol glycosides and 6% diterpene lactones."

Gafner added: "Ginkgo adulteration has become rather sophisticated. For some of the commercial samples, it is difficult to determine if the ginkgo extract is adulterated, or if the discrepancies from the regular ginkgo leaf extract fingerprint are due to differences in the manufacturing process or inadequate storage conditions."

The cranberry and ginkgo bulletins are the 37th and 38th peer-reviewed publications, respectively, published by the program. As with all publications of the program, the bulletins are freely accessible to all ABC members, registered users of the ABC website, and all members of the public on the program's website (registration required). HG

**—ABC Staff**

Botanical Adulterants Prevention Program

BOTANICAL ADULTERANTS BULLETIN

Adulteration of *Ginkgo biloba* Leaf Extract

By Stefan Gafner, PhD*

*American Botanical Council, 6200 Manor Road, Austin, TX 78723*

**Corresponding author:* email

**Keywords:** adulterant, adulteration, *Ginkgo biloba*, ginkgo leaf extract, Japanese pagoda tree, Japanese sophora, kaempferol, quercetin, rutin, *Sophora japonica*, *Styphnolobium japonicum*

Goal: The goal of this bulletin is to provide timely information and/or updates on issues of adulteration of ginkgo (*Ginkgo biloba*) leaf and ginkgo leaf extracts to the international herbal industry and extended natural products community in general. It is intended to give a brief overview on the occurrence of adulteration, known adulterants and analytical means to detect them, the market situation, and consequences for the consumer and the industry.

**1. General Information**

**1.1 Common name:** Ginkgo[1]

**1.2 Other common names:**

*English:* Maidenhair tree[1,2]

*French:* Ginkgo, arbre aux quarante écus, noyer du Japon[3]

*German:* Ginkgo, Fächerblattbaum, Mädchenhaarbaum, Elefantenohrbaum, Tempelbaum[3]

*Italian:* Ginkgo, ginko, ginco, albero di capelvenere

*Spanish:* Ginkgo, árbol sagrado, árbol de las Pagodes, árbol de los quarantos escudos

*Chinese: yin xing* (银杏)[4]

**1.3 Accepted Latin binomial:** *Ginkgo biloba* L.[1]

**Ginkgo**
*Ginkgo biloba*
Photo ©2017 Steven Foster

*Ginkgo biloba* - Botanical Adulterants Bulletin • *January 2018* • www.botanicaladulterants.org

1

# Korean Red Ginseng Provides Immune Support to Patients with HIV-1

**Reviewed: Cho Y-K, Kim J-E. Effect of Korean red ginseng intake on the survival duration of human immunodeficiency virus type 1 patients. *J Ginseng Res.* April 2017;41(2):222-226.**

Human immunodeficiency virus type 1 (HIV-1) is characterized by chronic inflammation and a progressive loss of T-cells (a type of white blood cell involved in immune response). Individuals with untreated HIV-1 have an estimated life expectancy of 11 years or less after diagnosis. HIV-1 is often treated with highly active antiretroviral therapy (HAART), but HAART may have adverse side effects. HIV-1 may develop resistance to HAART treatments over time, as well.

The authors of this study hypothesized that an alternative approach using Korean red ginseng (KRG; *Panax ginseng*, Araliaceae) root may provide protection for T-cells. Red ginseng is prepared by steaming freshly harvested, cultivated, naturally white- or cream-colored ginseng roots, which are usually four to six years old. This steaming process produces changes in the chemistry of the ginseng roots.

Since 1991, the authors have been conducting a longterm study on the effects of KRG in patients with HIV-1. (Patients began taking KRG after their first post-diagnosis measurement of CD4+ T-cells, a subtype of T-cells also known as T-helper cells.) This retrospective analysis sought to determine if the use of KRG could support and improve immune function in patients with HIV-1 prior to treatment with HAART drugs. The authors found that daily intake of KRG (Korea Ginseng Corporation; Seoul, South Korea) was associated with a slower decrease in CD4+ T-cells and increased overall longevity in patients with HIV-1.

| Study Details: At a Glance | |
|---|---|
| **Participants** | • 252 men and women<br>• Diagnosed with HIV-1 |
| **Study Design** | Retrospective study |
| **Study Length** | Retrospective analysis beginning in 1991 |
| **Test Material** | Capsules containing Korean red ginseng root (Korea Ginseng Corporation; Seoul, South Korea) |
| **Control** | No treatment |
| **Financial Disclosures** | Funding was provided by a grant from The Korean Society of Ginseng (publisher of the *Journal of Ginseng Research*), which receives financial support from the supplier of the test material. |

**Korean Red Ginseng** *Panax ginseng*
Photo ©2018 Steven Foster

Of the 252 patients included in the analysis, 162 received KRG and 90 patients did not (the control group). Patients were categorized by their total monthly intake of KRG (0 g, 30 g or less, or more than 30 g) and by the amount of time between their diagnosis and the last CD4+ T-cell measurement taken before starting HAART (more or less than 10 years), which the authors referred to as the "survival duration." According to the authors, the "introduction of HAART is recommended when the CD4+ T-cell count falls to 200-350/μL." (However, according to current guidelines from the US Department of Health and Human Services, HAART is recommended for all individuals with HIV, regardless of CD4+ count.[1])

While initial T-cell baseline counts were not significantly different among all patients, those receiving any dose of KRG had a significantly slower average annual decrease in CD4+ T-cell counts compared to the control group ($P < .001$). In addition, the time between HIV-1 diagnosis and the beginning of HAART was significantly longer in patients taking any dose of KRG compared to the control group ($P < .001$). Neither the rate of decrease in CD4+ T-cells nor the survival


DESIGN : MSLK

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rate differed significantly between the high-KRG (more than 30 g per month) and low-KRG (30 g or less per month) dosages.

This results of this study corroborate the use of KRG for immune support for patients with HIV-1. However, specific details about the KRG root used in this study were not included, which is a significant shortcoming. Also, other studies have found that, compared to KRG, Chinese red ginseng possesses comparable percentages of ginsenosides but generally has a greater percentage of polysaccharides, which may be worth exploring further. The authors also note that demographic and lifestyle factors were not taken into account in this study, which should be controlled for in future studies. HG

**—Kathleen Bennett**

## Reference

1. Guidelines for the use of antiretroviral agents in adults and adolescents living with HIV. National Institutes of Health website. Available at: https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv/10/initiation-of-antiretroviral-therapy. Accessed January 25, 2018.

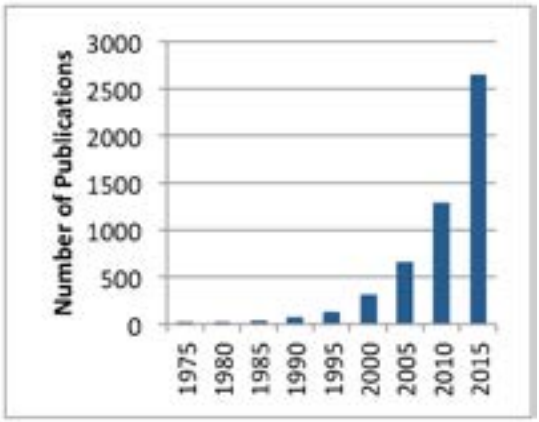
**Korean Red Ginseng** *Panax ginseng*
Photo ©2018 Steven Foster

# Scientific Journals Increasingly Skeptical of Antioxidant Research

**In its December 2017 issue, *The Journal of Food Composition and Analysis* (JFCA) published an editorial in which it announced that the journal "will no longer accept papers for review that employ antioxidant and total phenolic assays."[1]**

The JFCA's new policy follows a trend started by other scientific journals that focus on natural products research and that no longer accept or restrict acceptance of papers dealing with antioxidant activity of extracts or isolates from plant, fungal, or animal sources. The *Journal of Ethnopharmacology* lists "in vitro antioxidant activity" as a rejection criterion, stating that such activity is "present in all plants" and thus is less meaningful without additional data.[2] *Planta Medica* and *Fitoterapia* also reject manuscripts that report predictable biological activities, such as the antioxidant activities of phenolic compounds.[3,4]

**Figure 1. Number of Papers in PubMed with 'Antioxidant Activity' in Title or Abstract, 1975-2015**




In his editorial, JFCA Editor-in-Chief James Harnly, PhD, a research leader at the United States Department of Agriculture's Food Composition and Methods Development Laboratory, notes that there is little evidence that antioxidant activities observed in vitro will have an impact on health in animal or human studies.[1] In addition, the tests used to measure total antioxidant activity, such as the ORAC, DPPH, TEAC, and FRAP† assays, are non-specific and prone to interferences, and therefore do not provide reliable results. As a consequence, the JFCA will immediately reject papers in which the data primarily rely on these assays. For manuscripts that use these assays to provide additional data (e.g., to explain a mechanism of action), the JFCA will request that the authors resubmit the paper after omission of the antioxidant data.[1]

Interest in antioxidant activities started to grow in the late 1990s because of data that established the involvement of reactive oxygen species (ROSs) in a number of major health issues (e.g., inflammation, cardiovascular disease, and cancer). The theory was that since antioxidants were able to react with these ROSs in vitro, they might lead to the development of agents capable of preventing some of the related health issues in humans. According to PubMed — the extensive medical database maintained by the US National Library of Medicine (a part of the US National Institutes of Health) — the number of papers containing the term "antioxidant activity" in the title or abstract has skyrocketed over the past two decades (Figure 1).

The usefulness of the data published on antioxidant activities is rightfully a matter of debate in the scientific community. Phenolic compounds, which play an important role in plant defense mechanisms, occur widely in the plant kingdom.[5,6] Plant defense mechanisms are activated in response to plant pathogens, injury, or environmental factors.[5-7] The increase in the concentration of ROSs is one of the initial defense reactions observed in plants. In order to avoid damage caused by the increased concentrations of ROSs, plant tissues use an array of antioxidant mechanisms, including enzymes and antioxidant secondary metabolites.[5,6] While these antioxidant compounds play an important physiological role in plants, much of their impact on human health has yet to be demonstrated.

Many dietary supplement and conventional food manufacturers have products with antioxidant claims in their portfolio (e.g., nutrition bars and antioxidant beverages), and the increased skepticism about the value of results from in vitro antioxidant assays may have an impact on these claims.[8] It may become less enticing for companies to make such claims if a majority of the scientific community concludes that such data are meaningless, or — as written in the editorial — that "'antioxidant' is a marketing term of questionable health and analytical value."[1] HG

**—Stefan Gafner, PhD**

## References


1. Harnly J. Antioxidant methods. *J Food Comp Anal.* 2017;64(Part 2):145-146.
2. The "Rules of 5." *Journal of Ethnopharmacology* website. Available at: www.elsevier.com/__data/promis_misc/jeprulesof5.pdf. Accessed January 5, 2018.
3. Guide for authors. *Fitoterapia* website. Available at: www.elsevier.com/journals/fitoterapia/0367-326x/guide-for-authors. Accessed January 8, 2018.
4. Guidelines for authors: editorial policy. *Planta Medica* website. Available at: www.thieme.com/media/ita/pubid-1019644585.pdf. Accessed January 8, 2018.
5. Kulbat K. The role of phenolic compounds in plant resistance. *Biotechnol Food Sci.* 2016;80(2):97-108.
6. Lattanzio V, Lattanzio VMT, Cardinali A. Role of phenolics in the resistance mechanisms of plants against fungal pathogens and insects. In: Imperato F, ed. *Phytochemistry: Advances in Research*. Kerala, India: Research Signpost; 2006:23-67.
7. Morales LO, Tegelberg R, Brosché M, Keinänen M, Lindfors A, Aphalo PJ. Effects of solar UV-A and UV-B radiation on gene expression and phenolic accumulation in *Betula pendula* leaves. *Tree Physiol.* 2010;30(7):923-934.
8. ORAC values might be passé, but antioxidant activity still demands research, experts say. William Reed Business Media, Inc.; 2017. Available at: www.nutraingredients-usa.com/Article/2017/08/15/ORAC-values-might-be-passe-but-antioxidant-activity-still-demands-research-experts-say. Accessed January 2, 2018.


† ORAC: Oxygen Radical Absorbance Capacity; DPPH: 2,2-Diphenyl-1-picrylhydrazyl; TEAC: Trolox Equivalent Antioxidant Capacity; FRAP: Ferric Reducing Antioxidant Power

# Single-Ingredient Clinical Trials with Tulsi: Systematic Review of the Evidence

**Reviewed: Jamshidi N, Cohen MM. The clinical efficacy and safety of tulsi in humans: a systematic review of the literature. *Evid Based Complement Alternat Med*. 2017;2017:9217567. doi: 10.1155/2017/9217567.**

| Study Details: At a Glance | |
|---|---|
| **Participants** | • 26 clinical trials<br>• 1,111 subjects (total)<br>• 10-80 years of age |
| **Study Design** | Systematic review |
| **Study Length** | 2-13 weeks |
| **Test Material** | Various tulsi preparations |
| **Control** | Various |
| **Financial Disclosures** | One author (Cohen) is a consultant and advisor to Organic India Pty. Ltd., a manufacturer and distributor of tulsi products. |

Tulsi (*Ocimum tenuiflorum*, syn. *O. sanctum*, Lamiaceae), also called holy basil, and East Indian basil (*O. gratissimum*) are aromatic culinary and medicinal herbs indigenous to India that have been used in the Ayurvedic traditional medicine system for more than 3,000 years. Tulsi includes two botanically and phytochemically diverse cultivars: Rama tulsi and Krishna tulsi. Tulsi and East Indian basil, which have similar traditional uses, can be distinguished from other *Ocimum* species by their bright yellow pollen, high levels of eugenol (among other phytochemical differences), and fewer chromosomes.

The *Indian Materia Medica* lists tulsi leaf extract as a treatment for bronchitis, rheumatism, and fever.[1] Tulsi leaf extracts also traditionally have been used to treat epilepsy, asthma, hiccups, skin and blood diseases, parasitic infestations, neuralgia (facial nerve pain), headache, wounds, and inflammation, and to maintain oral health. The leaf juice has been used to relieve earache, and leaf infusions have been used for stomach and liver disorders. Preparations of the roots and stems are used to treat mosquito and snake bites, and for malaria.

Since 2007, tulsi has been the subject of more than 100 scientific publications. In vitro studies suggest that tulsi leaf has adaptogenic, metabolic, immunomodulatory, antitumor, anti-inflammatory, antioxidant, hepatoprotective, radioprotective, antimicrobial, anticonvulsant, anxiolytic, and antidiabetic properties. In vivo, tulsi preparations have been shown to have anti-stress effects and to protect rats from stress-related cardiovascular changes. Human studies of tulsi leaf in multi-herb formulas previously have been reviewed systematically. This is the first critical systematic review of tulsi as a single-herb agent in human clinical trials, according to the authors.

The authors searched electronic databases from inception through November 2016 for human clinical trials of tulsi mono-preparations with at least one clinical outcome. Only English-language reports were included. Studies were excluded if they reported only on topical applications. After screening 1,553 reports, 31 met the inclusion criteria. Four papers were inaccessible, one reported on two independent clinical trials, and three publications were based on the same clinical trial, leaving 26 trials for review. (The abstract, article text, and flow chart state there are 24 trials, but the tables appear to list a total of 26 trials.)

## Study Details

The reviewed trials included a total of 1,111 subjects (10-80 years of age) and ranged in duration from two to 13 weeks. Most trials included subjects with acute or chronic illnesses, and only three studies used healthy subjects. In addition, only three studies had 100 or more subjects.

The following tulsi preparations and dosages were used: aqueous leaf extract (300-3,000 mg one to three times daily), methanolic leaf extract (300-1,000 mg twice daily), whole plant aqueous extract (6-14 g daily), fresh leaf aqueous extract (10 g daily in four equal doses), and tincture (30 drops daily in three equal doses). Two studies described the species or variety of tulsi used (Krishna, the purple-leafed cultivar of *O. tenuiflorum*, for both), and all others referred to tulsi as *O. sanctum*. Four studies compared tulsi with other herbal preparations, including curry (*Murraya koenigii*, syn. *Bergera koenigii*, Rutaceae) leaves, neem (*Azadirachta indica*, Meliaceae), a wild rosemary (*Rosmarinus* sp., Lamiaceae) tincture, and spinach (*Spinacia oleracea*, Amaranthaceae) leaf powder.

Only eight studies had a placebo group. Studies were randomized controlled trials (RCTs), non-placebo-controlled trials, or did not include randomization or control information. Jadad scores (a scale that ranks the methodological quality of a study) were generally low (0-3 points), and only three studies had high scores (4-5).

Outcome measures included blood glucose levels (eight studies), lipid profiles (six studies), immune response (six studies), neurocognitive changes (four studies), mood (three studies), fatigue (two studies), uric acid levels (two studies), secondary symptoms of diabetes (one study), and "sleep problems" (one study). A majority of reports stated that no adverse events (AEs) occurred; one reported mild, occasional nausea; and the rest did not mention AEs.

## Results

### *Metabolic Conditions*

Of the 17 studies on metabolic conditions, 10 assessed tulsi's effects on blood glucose, lipids, and blood pressure in subjects with type 2 diabetes or metabolic syndrome, and only one reported on tulsi's effects on clinical symptoms of type 2 diabetes. Six of the studies on metabolic syndrome were RCTs. In addition, one study reported on obesity, and two investigated uric acid changes in subjects with gout. Six of the studies on metabolic conditions were between 12 and 13 weeks long (the rest were shorter). Trials lasting 12-13 weeks showed more dramatic changes in fasting blood glucose and postprandial glucose levels than trials of four to five weeks. In one study, hemoglobin A1c, a marker for blood glucose levels, significantly decreased with tulsi and hypoglycemic medication (the active comparator) compared to the medication alone. In studies of both healthy subjects and subjects with diabetes, there were significant improvements from baseline in fasting blood glucose, postprandial glucose, urine glucose, uric acid levels, and lipid profiles for those in the tulsi groups. Improved blood pressure was reported in some but not all studies. Improved body mass index was reported in obese subjects.

### *Immune Response and Inflammatory Conditions*

Five studies reported enhanced immune response in subjects taking tulsi. Two studies included patients with acute viral infections, one involving encephalitis and the other hepatitis. In the study on encephalitis, subjects taking the tulsi preparation demonstrated higher survival rates after four weeks compared to those taking dexamethasone. In the hepatitis study, subjects in the tulsi group reported symptom relief after two weeks compared to baseline. In patients with asthma, tulsi improved vital capacity and relieved symptoms in three days.

### *Mood and Cognition*

Four studies on neurocognitive effects reported significant improvements in mood and/or cognition for those who consumed tulsi regardless of their age or gender, or of the formulation or dose used. In three studies, there were significant reductions in anxiety and stress for those who consumed higher tulsi doses for longer periods.

## Conclusion

The authors concluded that the reviewed studies "suggest that tulsi is a safe herbal intervention that may assist in normalizing glucose, blood pressure and lipid profiles, and dealing with psychological and immunological stress." Tulsi's effectiveness across diverse clinical domains suggests an adaptogenic effect. The Ayurvedic tradition of consuming tulsi daily (either on an acute or a chronic basis) may be an effective lifestyle measure to combat stress-related chronic illnesses. More and better-designed RCTs are needed. HG

**—Mariann Garner-Wizard**

## Reference

1. Nadkarni KM, Nadkarni AK. *Indian Materia Medica with Ayurvedic, Unani-Tibbi, Siddha, Allopathic, Homeopathic, Naturopathic & Home Remedies*. Vol 2. 3rd ed. Mumbai, India: Popular Prakashan Private Ltd; 1982.

**Tulsi** *Ocimum tenuiflorum*
Photo ©2018 Steven Foster

# Traditional Chamomile and Sesame Oil Product Improves Mild-to-Moderate Carpal Tunnel Syndrome in Short-term Use

**Reviewed: Hashempur MH, Ghasemi MS, Daneshfard B, et al. Efficacy of topical chamomile oil for mild and moderate carpal tunnel syndrome: A randomized double-blind placebo-controlled clinical trial. *Complement Ther Clin Pract*. February 2017;26:61-67.**

| Study Details: At a Glance | |
|---|---|
| **Participants** | • 86 men and women<br>• Mean age of 43.7 (test group) and 41.9 (control group) years<br>• Diagnosed with mild-to-moderate carpal tunnel syndrome |
| **Study Design** | Randomized, controlled trial |
| **Study Length** | Four weeks |
| **Test Material** | Topical oil containing 1% chamomile essential oil and sesame oil (author-prepared) |
| **Control** | Placebo oil containing 10% sesame oil and 0.1% chamomile essential oil |
| **Financial Disclosures** | None |

Carpal tunnel syndrome (CTS) is characterized by tingling, numbness, and weakness in the hand. Treatments include surgery, splinting, nonsteroidal anti-inflammatory drugs, and corticosteroids. In traditional Persian medicine (TPM), chamomile (*Matricaria chamomilla*, syn. *M. recutita*, Asteraceae) is considered an analgesic agent. In particular, chamomile flower extract is used as a topical treatment for joint pain. The authors of this study have previously reported that a standardized formulation of chamomile oil has been found to be beneficial in severe CTS. The purpose of this randomized, double-blind, placebo-controlled study was to evaluate the preparation's effects on symptoms of mild-to-moderate CTS.

Patients over the age of 18 who met electrodiagnostic criteria for mild-to-moderate CTS were recruited from outpatient clinics of Shahid Faghihi Hospital and Imam Reza Polyclinic in Shiraz, Iran, between August 2014 and February 2015. Electrodiagnosis is a diagnostic method in which the body's natural electrical activity, or the body's response to an external electrical stimulus, is measured. Mild-to-moderate CTS was defined using various electrodiagnostic criteria, including compound latency, which is the time between nerve stimulation of a muscle and its response.

Included patients had at least two of the following symptoms: numbness, paresthesia (burning or prickling sensation on the skin), nocturnal pain, tingling, and positive Phalen, Tinel, or compression tests (assessments used in the diagnosis of CTS). Exclusion criteria were as follows: severe CTS; previous wrist trauma, fracture, or surgical release of the median nerve; intracarpal injection within six months of the study; cervical radiculopathy (pain caused by damage to a nerve root in the cervical spine) detected by electromyography; recent use of analgesics or corticosteroids; hypersensitivity to the study treatments; inability to complete the data-gathering sheet; neuropathy; collagen vascular diseases; rheumatoid arthritis; hyperthyroidism; diabetes; renal failure; and alcoholism.

The treatment preparation was made by the researchers. Chamomile flowers were purchased from a traditional herbal shop in Shiraz, Iran. The flowers were obtained from the nearby city of Kazeroon and were morphologically authenticated. The preparation method was based on historical medical literature. Powdered chamomile flower was boiled in distilled water, then the plant residue was removed and the resulting liquid was combined with sesame (*Sesamum indicum*, Pedaliaceae) seed oil (Golkaran Co.; Mashhad Ardehal, Kashan, Iran) and boiled until the water was removed. The authors note that the preparation contained 1% chamomile essential oil. The essential oil was analyzed by gas chromatography-mass spectrometry and the main components were found to be bisabolone oxide A (62.4%), bisabolol oxides A and B (15.5 and 2.1%, respectively), and β-caryophyllene (7.5%). The placebo was 10% (by volume) sesame oil in pharmaceutical paraffin with 0.1% hydrodistilled chamomile essential oil. The authors state that the rationale for including a small amount of chamomile in the placebo was to convey chamomile odor to help maintain blinding.

All patients were instructed to wear a wrist splint to immobilize the wrist at night. Every morning and evening, patients were instructed to place five drops of the treatment or placebo on the palmar area of the wrist for four weeks. They also were instructed not to massage the wrist. The primary outcome measure, which was assessed at the beginning and end of the study, was the Persian version of the Boston Carpal Tunnel Questionnaire, which assesses function and symptom severity.

Of 112 assessed patients, 86 were enrolled in the study, and 43 were randomly assigned to the treatment or placebo group. Because nine patients were lost to follow-up, 39 completed the study in the chamomile group and 38 in the placebo group.

The improvement from baseline was significantly greater in the chamomile group than in the placebo group for symptom severity ($P = .017$), functionality ($P = .0001$), and

dynamometry (a measurement of muscle power), for which the mean score slightly worsened in the placebo group ($P$ = .040). Compound latency of the median nerve significantly improved in the chamomile group compared with the placebo group ($P$ = .035). There were no other significant changes in electrodynamic measurements. No patients reported any adverse effects.

The authors concluded that four weeks of traditional chamomile oil treatment can improve symptoms and function in patients with mild-to-moderate CTS. It should be noted that sesame oil has been shown to have antioxidant, anti-inflammatory, and anesthetic properties. Therefore, the benefits seen in this trial cannot be attributed to chamomile alone. The chamomile oil and sesame oil could be working additively or synergistically. Limitations of the study include the short study duration (given that CTS is a chronic condition) and relatively small sample size. Nonetheless, this study provides support for the benefits of this treatment in CTS. HG

**—Heather S. Oliff, PhD**

**Chamomile** *Matricaria chamomilla*
Photo ©2018 Steven Foster

# From the Desk of **James A. Duke**

**By Helen Lowe Metzman**

**It is daunting to be sitting at the legendary Dr. James A. Duke's desk typing this tribute to him. It is even more disconcerting to be here in Jim's basement library/office without him hunting and pecking away with his index fingers. I am surrounded by Jim's wealth of books and his articles, poetry, and prose stuffed inside government-issued file cabinets that line the side wall.**

How I wish I could hear just one more story, like the story of his dangerous flight over Jamaica searching for *ganja* (*Cannabis* spp., Cannabaceae) fields, or the story of going to Iran seeking Persian poppies (*Papaver bracteatum*, Papaveraceae) to replace opium poppies, or going down the Shenandoah and discovering Sweet Annie (*Artemisia annua*, Asteraceae) at pit stop number two, or the tale of traveling to China to find the Chinese fountain of youth.

"Ginseng"

*Searching for the Holy Grail*
*On the Appalachian trail,*
*When I found the herb they call ginseng.*
*Growing deep down in the woods,*
*That's where I got the goods,*
*That the Chinese call renshen.*

—From *Herbalbum: An Anthology of Varicose Verse* (1985)
by Jim Duke

This otherwise outdated office comes alive with Jim's artifacts. Vibrant red colorful fabric *molas* on the walls depicting cats, fish, demons, and the Mexican musician Antonio Aguilar are a reminder of his early beginnings as an enthobotanist.

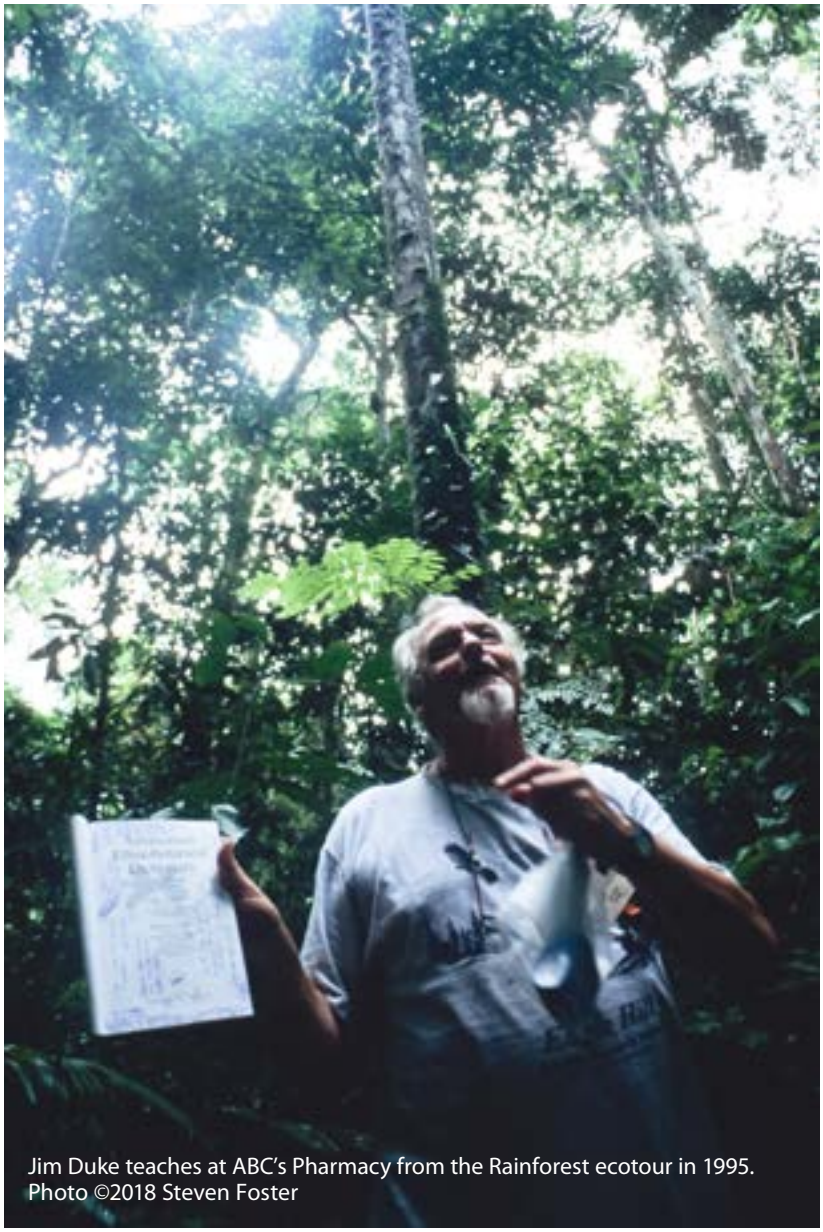
Watercolors of voluptuous Panamanian Chocó (now called Embera-Wounaan) women opposite his desk are lovely to gaze at but also a reminder of what a charmer this man was.

Over the never-used brick fireplace in the corner is a highly textured expressionist painting of Jim playing a bass that grows out of tree roots.

Photos on the wall of his band, The Howard County Dump, conjure images of Jim working steadily on his computer while listening to classical, jazz, and bluegrass on his static radio and when he religiously listened to *G-Strings* on WPFW every Sunday morning.

The complete volume set of *The Wealth of India,* botanical references that span the globe, pharmacognosy books, nutritional books, edible plant and mushroom books, as well as many of his own publications are currently shelved, neat and tidy, even though just a few months ago they were strewn into collapsing piles when he worked tirelessly at his desk in this faded blue computer chair that I am presently occupying.

Jim did not care about the decorative properties of this basement grotto, where he spent so much time as a compiling troglodyte. He did not care one bit about aesthetics. He



Jim Duke teaches at ABC's Pharmacy from the Rainforest ecotour in 1995.
Photo ©2018 Steven Foster

was a man of the mind. Words mattered. Information mattered. Music mattered. Plants mattered. Family and friends mattered. Teaching and telling stories mattered, as did trying repeatedly to get the US Food and Drug Administration (FDA) to get fair, comparable trials of North American and all medicinal plants, alongside "Big Pharma" and placebos.

Walks in the woods identifying local flora mattered. Saving the Amazonian rainforest mattered. Getting folks outdoors and promoting healthy food "farmacy" mattered.

He was a tome, a walking encyclopedia with a genteel southern drawl that fluctuated between refined and redneck. Women would peel off their shirts down to their undies in our classes for him to urticate, or flagellate, their arthritic backs with stinging nettles (*Urtica dioica*, Urticaceae). He dined on cicadas spiced with Old Bay seasoning. He ate live palm beetle larvae called *suri* grubs from the Amazon and coined the word "suriculture." He would stuff creeping charlie (*Glechoma hederacea*, Lamiaceae) up his nose to demonstrate how to ward off anthrax.

Jim wore necklaces of the bulbs of garlic (*Allium sativum*, Amaryllidaceae), the "stinking rose," to keep away the flu. He cooked Duke's soup du jour for the garden crew every day for years. He made mānuka honey antibacterial salves and concocted pomegranate (*Punica granatum*, Lythraceae) juice-based styptics to stop bleeding.

Jim's idea of a research study in the garden was to rub mountain mint (*Pycnanthemum muticum*, Lamiaceae) on only one of his legs for its pulegone phytochemical, walk through the woods, and see which leg ticks preferred. Jim taught us about the explosive seed dispersal of the jewelweed (*Impatiens capensis*, Balsaminaceae), as well as the uses of horny goat weed (*Epimedium grandiflorum*, Berberidaceae). I'm not even going to discuss what he had to say about fava beans (*Vicia faba*, Fabaceae).

Jim dyed his hippie beard yellow with turmeric (*Curcuma longa*, Zingiberaceae) and chanted shamanic chants, *icaros*, "mucarita, mucarita," as he reflected on his experience with *La Soga* and the ayahuasca (*Banisteriopsis caapi*, Malpighiaceae) ceremony.

He formulated medicinal living liqueurs with clever labels like "Alzheimeretto," "Crème de'mentia," and "Hot-Bloodied Mary." He was always hot on the trail of the latest health issue or herbal discovery and would spend days crawling through PubMed data to either support or disclaim the information. He would, in his folksy yet scientific fashion, write plant rants suffused with long lists of phytochemicals of each species and continually update his USDA database to report his findings. Day after day, he broadcasted his rants via his enormous email contact list, interviews on radio shows, newspapers, videos, and to garden tours.

The beautiful botanical illustrations featured to the left and throughout the proceeding James A. Duke articles were done by Peggy Duke, Jim's wife, for the *ABC Clinical Guide to Herbs*. Peggy generously gave permission for them to be featured.

With his humble yet eloquent teaching style, Jim had a unique gift to make phytochemicals, traditional plant knowledge, and scientific research palatable to all, no matter their background. Universities, government organizations, garden clubs, homeschoolers, refined researchers, botanists, herbalists, hippies, and connoisseurs of wild edibles made their way to the garden not just to learn about plant medicine but primarily to meet Jim. He was often asked at the tours: "How did you get your interest in plants as food and medicine?"

Jim repeatedly said that he had a charmed life. He was born on April 4, 1929, in Birmingham, Alabama, just prior to the stock market crash. At age five, Jim was introduced to watercress (*Nasturtium officinale*, Brassicaceae) and chestnuts (*Castanea* spp., Fagaceae) after befriending the lonely old man across the street "who only had his rabbits to talk to." During the Great Depression, when he was eight, his family moved to Durham, North Carolina, where Jim became interested in wildflowers and enjoyed going to the woods so much that he worked at a state park in his teens as a junior park ranger. Music also filled his high school years. The guitar was his first interest as he learned to play hillbilly chords and then moved on to bass fiddle in Raleigh. He played with Homer A. Briarhopper and His Dixie Dudes and cut a record called the "Briarhopper Boogie" in Nashville. A singer-songwriter himself, Jim's songs were cut into a vinyl LP, *HerbAlbum,* in the 1980s. He played jazz, big band, blues, and bluegrass, and maintained his love of music with jam sessions at the house until his final days of ordering Amazon's "Alexa" to play his favorite tunes.

**With his humble yet eloquent teaching style, Jim had a unique gift to make phytochemicals, traditional plant knowledge, and scientific research palatable to all, no matter their background.**

After abandoning a music major his first semester at the University of North Carolina (UNC) at Chapel Hill, Jim eventually received three "academically inbred" degrees at UNC, including his PhD in botany. It was during his master's studies at UNC that he fell in love with Peggy-Ann Wetmore Kessler, who was also pursuing her master's degree in botany. Together, they shared botany and music and eventually married in 1961.

During his military service, Jim worked on culturing fungi and later understood his projects were for the purpose of developing biological agents with the potential of destroying enemy crops. Because of his time in the military, he received benefits from the GI Bill, and Jim returned to UNC, where he completed his PhD in 1961, and traveled to Mexico, Guatemala, and Costa Rica on plant-gathering expeditions. It was during this time that his infatuation with Latin America began. Jim moved to St. Louis to be at the Missouri Botanical Garden and

Washington University for his postdoctoral work as a taxonomist identifying dried herbarium specimens from Peru. Jim then traveled to Panama to identify and describe the best vegetation to support "vehicular traffic" before starting his career at the USDA in 1963.

Jim admitted that although he loved his work with plants, he did not always feel comfortable with the reason behind his work. For instance, early on in his career with the USDA, he studied plant succession in Puerto Rico, but it was for the purpose of learning how defoliants or herbicides alter that succession.

While at the USDA, Jim was offered a consultant job with the Battelle Memorial Institute in conjunction with the Atomic Energy Commission to work in Panama for two and half years. He accepted, left the USDA, and moved there with his young family including his "botanical illustrator par excellence" wife Peggy, their two-and-a-half-year-old son, John, and their six-month-old daughter, Celia.

Jim's assignment was to go off into the bush of Darién province to investigate and thoroughly document the flora and fauna as well as observe the Chocó (Embera-Wounaan) and Cuna (Guna) populations for what they were eating. There was a proposal to excavate a sea-level canal using nuclear weapons, but there were questions about whether radioactive materials would settle into the soil and how these materials might affect the indigenous populations and the local food chain. Ultimately, the project was tabled, and it was determined that it was not feasible to use nuclear weapons to excavate a canal.

The experiences of being in the Panamanian jungle impressed on Jim how deeply tied the indigenous populations were to their environment. Jim became a "Panamaniac," studying the food and medicine of the indigenous Chocó population. Jim often told groups of students that his time spent in Panama was the time when he metamorphosed from a taxonomic botanist to an "ethnobotanist" — a term he did not know at the time. From his observations, he noted the contrast of how indigenous people used herbs versus how his own family used conventional medicine. Jim concluded that there was better living through phytochemistry, not "pharmachemistry."

Back from Panama, Jim returned to Battelle in Columbus, Ohio, to document his findings, which led to a compilation of articles that resulted in one of his first self-published titles, *Isthmian Ethnobotanical Dictionary,* in 1972.

In 1971, Jim returned to the USDA, where he continued to work as an economic botanist and received assignments such as crop diversification and the challenging position of seeking alternative cash crops for cultivated narcotic plants, including coca (*Erythroxylum* spp., Erythroxylaceae), poppies (*Papaver* spp., Papaveraceae), and marijuana. He was appointed chief of the Medicinal Plant Resources Laboratory (1977), whose mission was to work with the National Cancer Institute (NCI) to collect plants that had potential antitumor activities. This position took him around the globe as he documented not only toxic plants but also traditional plant knowledge.

"Mayapple Lemonade"

*Penobscot Indians up in Maine*
*Had a very pithy sayin'*
*Rub the root most every day*
*and it'll take the warts away.*

*Farther south the Cherokee*
*echoing Menominee*
*Made a tea out of the roots*
*to keep the bugs off potato shoot.*

*Mayapple lemonade, wildest thing my momma made,*
*Coolest thing there in the shade, fruits of amber, leaves of jade.*

*They couldn't know etoposide,*
*nor of its aid to homicide*
*Nor could they know the course it charts,*
*for cancer of the private parts.*

*I'll venture to prognosticate*
*before my song is sung*
*This herb will help alleviate*
*cancer of the lung.*

*Mayapple lemonade, wildest thing my momma made,*
*Coolest herb in the summer shade, swing your partner'n promenade.*

—From *Herbalbum: An Anthology of Varicose Verse* (1985)

Jim's medicinal plant compilation led to the development of his USDA database that he continued to work on meticulously for decades. After the Reagan administration shut down his program with the NCI, Jim returned to specializing in alternative crops for narcotics. He continued work with this program while he simultaneously began teaching "Pharmacy from the Rainforest" ecotours in the Amazon, where he went at least 50 to 60 times. He lost count.

Jim retired one year early from the USDA in 1995 to write his Rodale bestseller *The Green Pharmacy*. The sales of his book enabled him to realize his dream and create the "Green Farmacy Garden" in his backyard. In 1998, Jim and Peggy converted a portion of their six-acre "Herbal Vineyard" farmette in Fulton, Maryland, into a teaching garden designed by John Snitzer and Kerry Kyde. The Green Farmacy Garden, with its 80 plots, represents the chapters of his book. These plots are designed to highlight plants associated with the treatment of conditions and ailments like Alzheimer's disease, prostate disorders, osteoporosis, high blood pressure, diabetes, yeast infections, constipation, and bacterial infections. In the garden, Jim taught about traditional uses of plants across our planet, botanical medicine research, and herbal alternatives to pharmaceuticals. He did so with credibility and debunked anything that he believed was a charlatan claim.

**Jim was a reductionist botanist who believed in the synergistic healing of the whole plant with its thousands of phytochemicals. Jim believed that our DNA has been commingling with plant constituents for thousands of years. Jim believed that when given herbs, our bodies will mine what constituents it needs. He fervently believed in the healing power of plants.**

"Hushpuppy: The Sad Sage of St. John"

*I remember that sad day*
*In the year 2002*
*When I heard the TV say*
*St. John ain't good for you.*
*I reckon they forgot*
*What you really oughta know*
*2 billion bucks of Zoloft*
*Placed second to placebo.*

—From *Herbalbum: An Anthology of Varicose Verse*, 3rd edition (2010)

Jim was famous for walking barefoot in his cut-off shorts that exposed his bowed legs. He had a disdain for cumbersome shoes, and if he did wear any, they were slip-ons with soft soles. This "barefoot doctor" led groups to the "Gout" plot and recalled how he used celery (*Apium graveolens*, Apiaceae) seed for his condition, and that the pharmaceutical colchicine was originally extracted from the autumn crocus (*Colchicum autumnale*, Colchicaceae).

He walked barefoot in the Amazon, too, while all of the rest of us on my trip in 2003 sported hiking boots, quick-dry safari pants and shirts, and gear to repel mosquitoes and avoid the venomous bite of the fer-de-lance. I'll never forget one afternoon when Jim called me into his open-air lodge room to show me blue morpho butterflies puddling or drinking minerals from mud right outside his window where he had dumped the contents of his nighttime chamber pot.

In the Amazon, Jim, along with the Peruvian guides, played not only the typical folk songs *de Colores* and *El Cóndor Pasa*, but also John Denver's *Take Me Home, Country Roads*. Jim wrote a parody to the tune of John Prine's *Paradise* with a dire warning that the state of the Amazon rainforest would be *Paradise Lost*.

"Paraside Lost"

*Daddy won't you take me to the Primary Forest*
*By the Amazon River where paradise lies?*
*I'm sorry my son, but the forest is gone!*
*I'll show you some slides, that will have to suffice!*

In addition to the ecotours to the Peruvian Amazon, Jim's work as an ethnobotanist offered him the opportunity to travel the world in search of medicinal plants while touching the hearts and minds of many, young and old. I was fortunate to have met Jim in my early thirties around 1991 and again in 1997, just after his *Green Pharmacy* was published and before the garden was installed in 1998. After the garden was built, I volunteered for several years under the guidance of the previous garden director, Holly Vogel. I am forever grateful that Holly asked me to work at the garden, as I got to know Jim and his plants as they aged with the garden.

I accompanied Jim to the Amazon, the United Plant Savers Sanctuary in Rutland, Ohio, Finca Luna Nueva Lodge in Costa Rica, Eagle Hill Institute in Maine, Black Mountain and Brevard in North Carolina, Wintergreen Resort in Virginia, and finally, to the country he always wanted to visit, Cuba. From watching Jim traipse muddy paths barefoot in the Amazon basin, to skinny-dipping with our Tai Sophia class in Ohio, to assisting him with his rollator on cobblestone streets in Cuba, Jim became not only my mentor but also my dear friend.

Jim, a proclaimed altar-boy-turned-atheist, claimed he did not believe in spirits. He did, however, talk about plant-to-plant communication from the aromatic spirits, methyl salicylates, of wintergreen (*Gaultheria procumbens*, Ericaceae). His tales were sprinkled with his ayahuasca vision of watching three women dressed in white taking notes in his garden, as well as a fellow participant, who in her vision, saw her brother die of a heart attack. Although he would never admit it, I have a hunch that Jim, the skeptic, became a believer of shamanic powers when, at the end of the tour, his student got back to the dock in Iquitos, Peru, and was handed a note to inform her that her brother had passed.

Jim was a reductionist botanist who believed in the synergistic healing of the whole plant with its thousands of phytochemicals. Jim believed that our DNA has been commingling with plant constituents for thousands of years. Jim believed that when given herbs, our bodies will mine what constituents it needs. He fervently believed in the healing power of plants.

After a bout with neuropathy in his legs, Jim started losing his ambulatory abilities and went from compiling away on his computer to a holding pattern, wanting to go. Jim was, in his own words, "waiting for the reaper to come and harvest me." An apropos metaphor for a botanist. Portending the inevitable, the garden's ayahuasca, La Soga, The Vine, which had looked healthy just a couple days before Thanksgiving, died a week before Jim. Could it be that "celestial connections" intertwined these two? He would say no; it was just coincidence. The last words he told me were that he "hates winter." Two days later the weather abruptly changed from a balmy late autumn to cold and snow. The reaper came, and Jim peacefully passed in his home on Sunday, December 10, 2017, eleven days before the winter solstice.

As I sit here at his desk, I must confess that I find solace imagining Jim in green pastures of a tropical paradise perpetually playing parodies, plucking plants, and waxing poetic varicose verse.

May his words, wisdom, and spirit continue to educate and inspire for decades, if not centuries, to come. HG

Jim Duke teaches at ABC's Pharmacy from the Rainforest workshop in 1995. Photo ©2018 Steven Foster

# JAMES A. DUKE

## *A Diverse Life of Botanical Bounty*

**By Steven Foster**

### Alabama-Born

James Alan Duke, PhD, was born in Birmingham, Alabama, on April 4, 1929, delivered at home by an African-American midwife. He was raised in the red clay hills outside of Birmingham, where one could find a Duke living on nearly every hill. "I come from the cotton-pickin' Dukes, rather than tobacco Dukes,"* he recalled with his always-present humor, accented by a soft-spoken cadence reflecting his Alabama roots. In his first six years, he spent time between his grandmother's home on Second Avenue in south Birmingham and a farm along the Coosa (Koosa) River about 40 miles outside the city with his parents and two brothers. His father was a cotton farmer, who later dabbled in the nursery and horticulture business.

Duke recalled that his family was "plain ol' poor" and they would eat what they could find or grow most of the time, usually homegrown and canned food shared by the extended Duke family in rural Alabama. In a February 1999 issue of *People* magazine, he mused that his family was "so poor we were *The Grapes of Wrath* and didn't know it."[1]

A favorite early culinary memory of Duke's was of scuppernong grapes, a native southern

* James B. Duke, 1856-1925, best known as the father of the modern cigarette, created "The Duke Endowment," a trust that would result in renaming Trinity College to Duke University. James A. Duke is not related to James B. Duke.

variety of the muscadine grape (*Vitis rotundifolia*, Vitaceae), which originates along the Scuppernong River of North Carolina. "It's a redneck grape like I'm a redneck person," Duke laughed. "They grew behind my grandmother's house and from late August until frost you could eat them off the vine." His grandmother often made scuppernong marmalade and jelly, but his favorite treat was the "treasure" his grandmother called "scuppernong juice."[2]

Across the street from his grandmother's Birmingham home lived Mr. Brooks, a lonely old man who kept rabbits. Duke, then five years old, believed that Mr. Brooks and the rabbits were his best friends. Old Mr. Brooks had a great love for nature and would take Duke to the hills along East Lake in Birmingham, where he learned about watercress (*Nasturtium officinale*, Brassicaceae) and chestnuts (*Castanea* spp., Fagaceae). By the time Duke started grade school, he had developed a love for biology and the music he heard in the Alabama countryside.

### North Carolina Upbringing

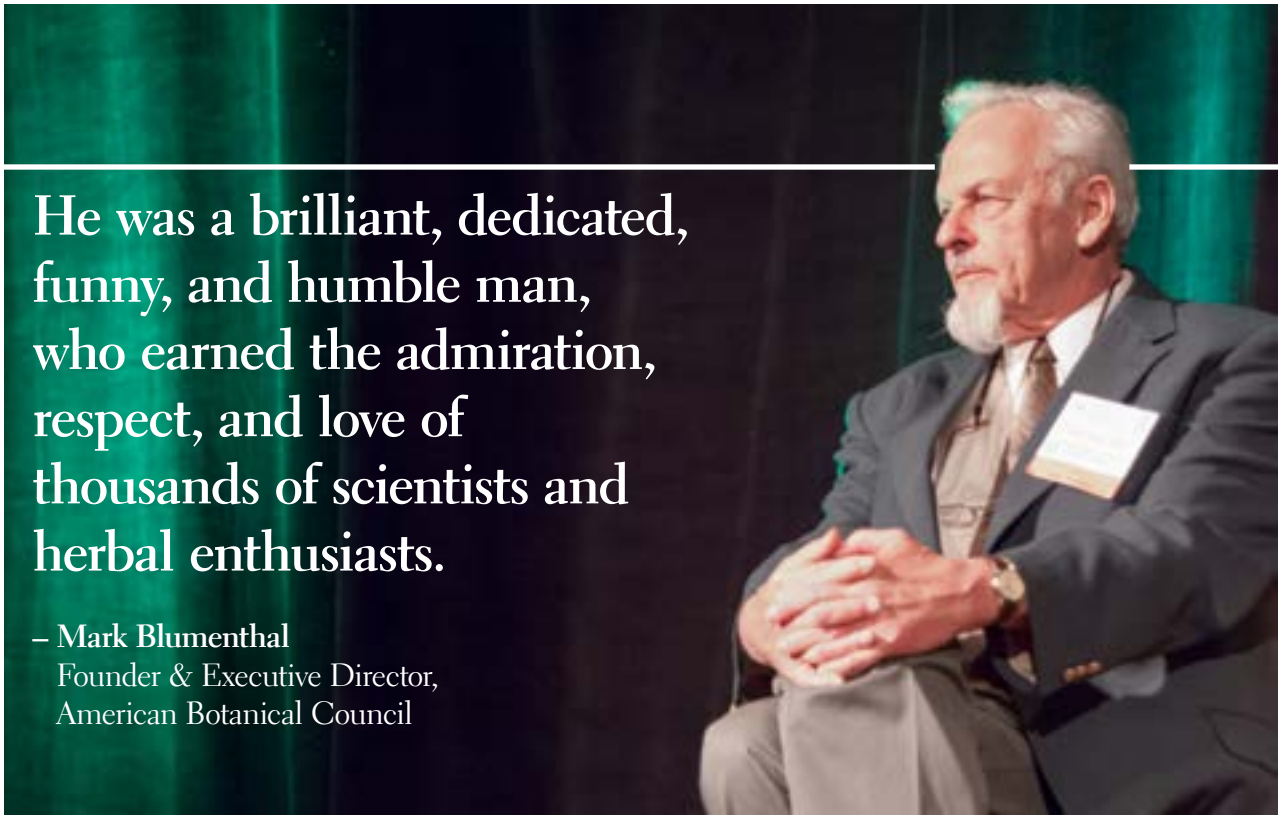
Duke lived in Alabama until he was eight, and the Great Depression years forced the family to move to Durham, North Carolina, with Duke and his two brothers in the "rumble seat of a very broken-down car."[3] His family lived in Durham for a year or two and then moved to Raleigh. His father became an insurance salesman, and the family prospered. His dad started playing golf, and the family ate meat and potatoes instead of the high-fiber, mostly vegetable-based diet that they had survived on in Alabama.

Years later, Duke recalled: "This is a story that's important to me. Both my father and his two brothers who died of cancer graduated from the rural high-fiber diet to the meat-and-potato diet of the newly affluent, and I really think that their cancers of the colon were due to this change in diet. I think that they would have lived many more years had they not achieved this level of affluence. I can't prove it. But I am what is called a high-fiber nut trying to avoid the same chain of circumstances."[3]

In a letter, dated April 15, 1993, to then-first lady Hillary Rodham Clinton, he repeated his position. "You asked for advice on your health reform program," Duke wrote. "Let me recommend one Jeffersonian health tidbit. If you must use meat, use it as a spice, not as a main entry. That could save thousands of lives and millions, if not billions of dollars."[4]

In Raleigh, Duke joined the Boy Scouts and became keenly interested in the outdoors and natural sciences, especially botany and biology.[3] Some of his teachers and mentors encouraged his obvious interest in the subject, including his mother, who got him a job watering plants at a greenhouse and enlisted his help in her flower garden. During the same time period, he had a magazine delivery route, and would sometimes trade magazines with musicians in exchange for a performance. His interest in southern folk music and plants grew in tandem.

From the age of 12 on, Duke spent long hours outside, taking hikes that were sometimes 10 miles or more. At age 15, a Mr. Jim Kessler got him a job as a "junior ranger" (really a glorified maintenance man, as Duke described it)




Jim Duke patiently waits while Mark Blumenthal introduces him to present the 2006 James A. Duke Excellence in Botanical Literature Award at the ABC Celebration during Expo West in Anaheim, California. Photo ©2018 Steven Foster

at what was then known as Crabtree Creek State Park and is now known as William B. Umstead State Park, a 5,088-acre park in the Raleigh-Durham area. The park was established in 1943 as one of the many Recreational Demonstration Area parks created by the National Park Service through the Works Progress Administration and the Civilian Conservation Corps.

The year 1944 was a formative one. By then, he had his own guitar, and, for three months, he lived in a one-room cabin with no water, electricity, or toilet in the middle of a broomstraw field at the park. It was here that he penned one of his first songs, inspired by observing the daughter of one of his bosses, whom he saw swinging on a porch with her blonde hair flowing with the swing's motion. That inspired the first verse of his "Chamomile" song, recorded on his 1986 vinyl LP *HerbAlbum*: "Golden hair up in a bun, smiling shyly in the sun." He never met the young lady.[5]

## Briars to Bands — From Bassist to Botanist

Duke married his first wife, a fellow musician, at a relatively young age. After reading Gene Stratton-Porter's *The Harvester* (Grosset and Dunlap), a 1911 novel featuring an herb wildcrafter, Duke dreamed of a Thoreau-like existence in the North Carolina mountains harvesting ginseng (*Panax* spp., Araliaceae). That fantasy meshed with his love of music, and Duke played bass fiddle with his wife's band (a trio featuring two sisters and their mother) on the then-country music station WBT radio in Raleigh that featured live country music and bluegrass programming. As a teenager he also played bass as a back-up musician with the trio at the Grand Ole Opry in Nashville, Tennessee.

While a student at E. Morrison High School in Raleigh, he played with another band. That gig took him to the WBT radio studio every morning at 6 a.m. to play bass fiddle for a 15-minute live music segment with Homer A. Briarhopper and His Dixie Dudes. In 1947, the young Jim Duke also went to Nashville with the group to record a 78-rpm record featuring the instrumental piece "The Briarhopper Boogie," in which Jim Duke played a bass solo.[3] Homer Drye's Briarhoppers and His Dixie Dudes with teenage bassist Jim Duke were mentioned in *Billboard Magazine* the same year.[6] The band, which formed in 1934, continues to perform as the WBT Briarhoppers, now in its ninth decade; the longest-lived bluegrass band of all time.[7]

After high school, Duke enrolled at North Carolina State University in a wildlife conservation program, but he soon dropped out. A year of working odd jobs, such as a carpenter's helper, sharpened his desire to return to school.[8]

His musical interests would lead to him to his career as a botanist. In the late 1940s, student musicians from the University of North Carolina (UNC) at Chapel Hill heard Duke playing bass and invited him to play with a big band jazz group at the university. In 1948, he enrolled in UNC as a music major and became the second bass player in the 20-piece jazz band. Since he didn't read music well, even though he had been practicing for five years, the first bassist played the notated music, while Duke was given the role of playing improvisational bass solos in the band for almost a decade.[8]

## Down the Botanical Garden Path

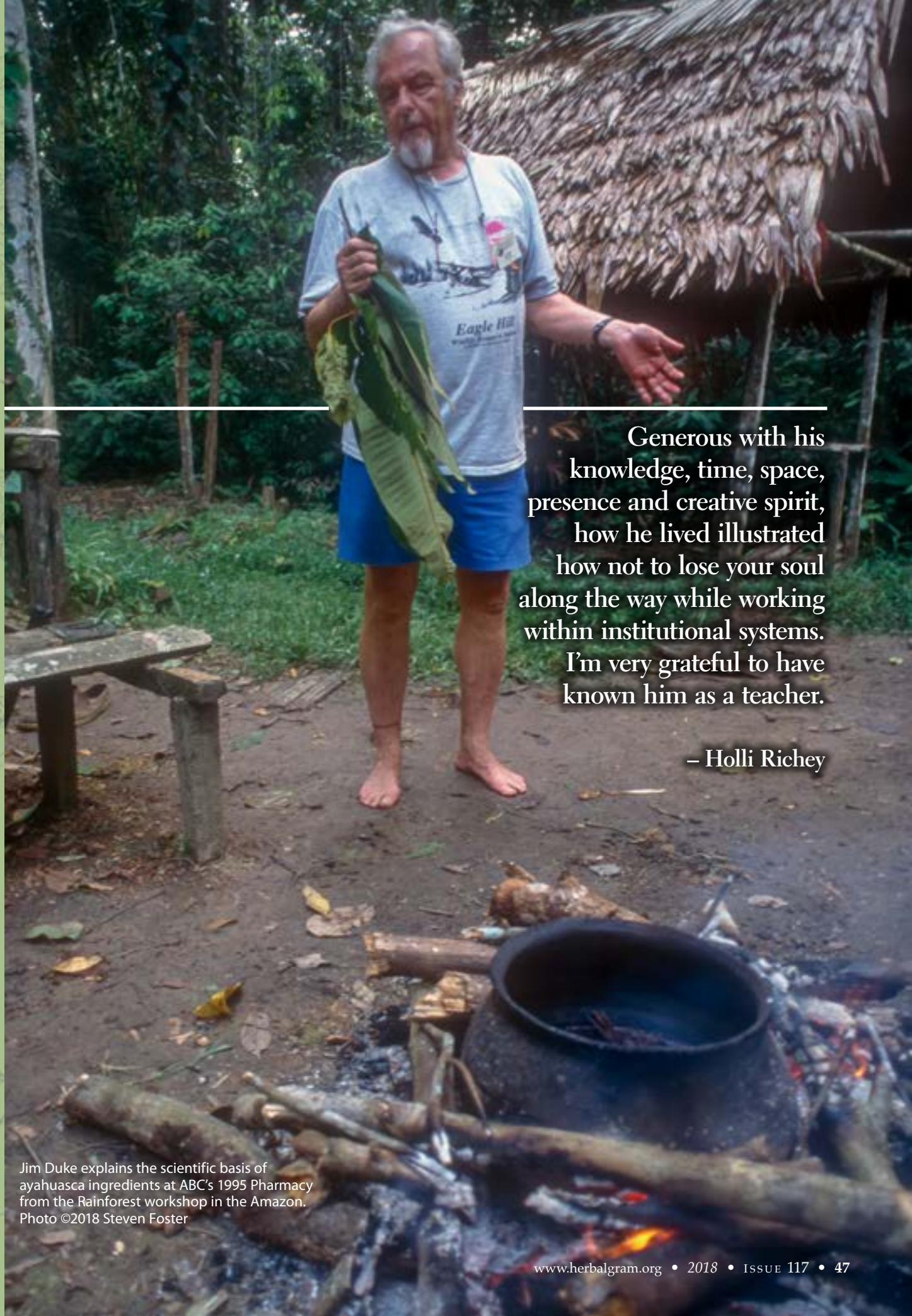
Duke's path to becoming a classical bassist went astray in his first semester at UNC. He took botany courses with H.R. Totten, PhD (1892-1974), and later with C. Ritchie Bell, PhD (1921-2013), and fell in love with field botany.[8] The experience compelled him to switch from a music major to a botany major with a focus on taxonomy and a minor in zoology. He earned his undergraduate degree at UNC in 1952. He continued on with a master's degree program in botany at UNC, where he met fellow botany student, Peggy-Ann Wetmore Kessler. They fell in love and married. Peggy K. Duke, a talented botanical illustrator, provided artwork for many of his publications.

Jim Duke attained his master's degree on December 7, 1955. The next day, on December 8, he was drafted into the US Army. He was sent to Fort Jackson in Columbia, South Carolina, for basic training, and then was stationed at Fort Sam Houston in San Antonio, Texas, located a few hours from the Mexican border. He recalled that on one of his three-day pass weekends he ventured across the Mexican border and got his first glimpse of Latin America, and fell in love with it. For the rest of his life, Duke would return to Latin America whenever he could.

The Army moved Duke to Fort Benning in Georgia and assigned him to the infantry.[8] Duke, of course, would have preferred to have been around plants, and he drafted a letter for his father to send to his Army officers explaining that he had a botany degree, and couldn't they put that to use? Not long after, he was transferred to Fort Detrick in Maryland, where he trained other soldiers about edible, useful, and poisonous plants and mushrooms.

After completing his two-and-a-half years of military service, he used the GI Bill to enroll in a doctoral program in plant taxonomy at UNC, and became the first graduate student of noted North Carolina botanist Albert E. Radford, PhD (1918-2006).[8] Radford, director of the UNC Herbarium from 1946-1983, co-authored the classic *Manual of the Vascular Flora of the Carolinas* with Harry E. Ahles and C. Ritchie Bell, published in 1968 by the University of North Carolina Press. Nearly every weekend during his PhD program, Jim and Peggy Duke were assigned to take Radford, Ahles, or Bell into the field to collect specimens for the *Manual.* The Dukes are honored in the "Acknowledgments" section of the book for their contributions, including their field collections.[9] The book was the first and only mid-20th-century technical flora guide for the South, is still a reliable reference, and remains in print today.

Duke enrolled in a PhD program in botany at UNC in 1959 and finished his PhD work in 1961, after which C. Ritchie Bell took him on the first of many botanical-collecting trips to Latin America.[10] The three-month excursion split time among Mexico, Guatemala, and Costa Rica, where they collected with Rafael Lucas Rodríguez Caballero (1915-1981), the iconic Costa Rican biologist, botanist, and artist known for his wildlife paintings, and for whom a wildlife sanctuary is named (*Refugio de Vida Silvestre Dr. Rafael Lucas Rodríguez Caballero*, Costa Rica).




Generous with his knowledge, time, space, presence and creative spirit, how he lived illustrated how not to lose your soul along the way while working within institutional systems. I'm very grateful to have known him as a teacher.

– Holli Richey

Jim Duke explains the scientific basis of ayahuasca ingredients at ABC's 1995 Pharmacy from the Rainforest workshop in the Amazon. Photo ©2018 Steven Foster

# "It was extremely interesting, learning how closely these people were tied to the environment."

Above photo: Duke and Ramón at the end of the Chiriquí Trail in Caldera-Quito, April 1968. Photo ©2018 Joseph H. Kirkbride, Jr.

Below photo: Duke in Río Teribe, Bocas del Toro, Panama, April 1968. Photo ©2018 Joseph H. Kirkbride, Jr.

## Distinguished Ecologist and Student of the Flora of Panama

After Duke completed all the botany courses and degrees offered at UNC in 1961, his professors suggested that he pursue postgraduate work with Robert E. Woodson, PhD (1904-1963), curator of the Herbarium at the Missouri Botanical Garden in St. Louis, Missouri. Woodson was working on a longterm publication project on the flora of Panama, and Duke put his taxonomic skills to work, writing treatments on Panamanian plant families. These include Amaranthaceae (amaranth family), Berberidaceae (barberry family), Caryophyllaceae (pink family), Ceratophyllaceae (hornwort family), Chenopodiaceae (goosefoot family), Monimiaceae (lemonwood family), Myristicaceae (nutmeg family), Nymphaeaceae (waterlily family), Polygonaceae (buckwheat family), and Ranunculaceae (buttercup family).

Duke's two years as a taxonomist and assistant curator at the Missouri Botanical Garden focused on identifying plant specimens collected in Panama and elsewhere in Latin America, including Peru.[10] During this period, Woodson served as a consultant for Ciba Pharmaceuticals, and they were collecting plants from Peru. Duke had the challenging job of trying to assign names to the Peruvian plant specimens. Although this was his first experience working specifically with medicinal plants, it was limited to the herbarium. It would also mark the end of his professional work as a taxonomist.†

In honor of Duke's taxonomic work on the Panamanian flora in the early 1960s, several species were named for him, including *Grias dukei* (now a synonym of *G. cauliflora*, Lecythidaceae),[11] *Koanophyllon dukei* (Asteraceae),[12] *Psychotria dukei* (now a synonym of *Notopleura dukei*, Rubiaceae),[13] and *Rondeletia dukei* (now a synonym of *Wittmackanthus stanleyanus*, Rubiaceae).[14] In 1966, John Duncan Dwyer, PhD (1915-2005), named a new genus in the Rubiaceae (madder) family *Dukea*, which included six species: *Dukea chariantha*, *D. panamensis*, *D. victoriae*, *D. blumii*, *D. darienensis*, and *D. euryphylla,* four of which were new to science. Dwyer named them "in honor of Dr. James Duke, distinguished ecologist and student of the flora of Panama."[15] Unfortunately, at least for those who would like to see Duke's name live on in botanical taxonomy, these species have since been relegated to synonymy in the genus *Raritebe*.

## Puerto Rican Plants

In 1963, Duke was approached by the Crops Research Division, a part of the US Department of Agriculture's (USDA's) Agricultural Research Service, for an assignment in Puerto Rico that piqued his interest. He took the assignment and traveled to Puerto Rico to study tropical tree

† Jim Duke's family treatments on the flora of Panama are published as 10 separate papers in various issues, volumes 47-49 (1961-1963), in the *Annals of the Missouri Botanical Garden.*

Duke with a local native, Loro, and his family in Manene, Darién, Panama, April 1968. Photo ©2018 Joseph H. Kirkbride, Jr.

seedlings. Specifically, the job involved experimental work and documenting how herbicides affected the succession of tropical vegetation. He became proficient at identifying tropical woody plants in the seedling stage.

One publication from this period proved useful in helping to identify tropical tree seedlings in Puerto Rico following the devastation caused by Hurricane Maria in September 2017. The comprehensive paper, "Keys for the identification of seedlings of some prominent woody species in eight forest types in Puerto Rico," also included 182 technical illustrations of seedlings by Peggy Duke.[16] The research was contracted by the USDA and sponsored by the Defense Advanced Research Projects Agency (DARPA) of the US Department of Defense. Peggy Duke's illustrations were prepared and subsidized by the Rain Forest Project of the Puerto Rico Nuclear Center in El Verde, Puerto Rico, and supported by the Division of Biology and Medicine of the US Atomic Energy Commission.[10]

## Panamanian Ethnobotanical Passion

After two years of successful research in Puerto Rico, Duke was offered a position as a research ecologist with the Columbus Laboratories of the Battelle Memorial Institute in Columbus, Ohio.[10] His assignment was to conduct bioenvironmental and radiological safety feasibility studies in remote regions of Panama. President John F. Kennedy had initiated a feasibility study to assess the practicality of widening the Panama Canal, or perhaps excavating a new canal, to accommodate supertankers. The project was called the Atlantic-Pacific Interoceanic Canal Study Commission. The United States had a tool that would easily accomplish the excavation work: nuclear devices. The idea was to detonate nuclear devices on the Central American isthmus to create a new canal from the Atlantic to the Pacific. Sponsored by the Atomic Energy Commission, Battelle was tasked with determining what radionuclides might get into the food chain if a new sea-level Panama Canal were to be excavated with nuclear devices.

"The dietary studies in Panama and Colombia were designed to quantify per-capita food consumption so that it could be determined what quantity of radionuclides would be ingested by natives following nuclear excavations of a sea-level canal, assuming that natives are allowed to return after a selected period of time," Duke explained.[17]

Duke's research took on an ethnobotanical and ethnozoological focus.[10] For nearly three years, his job was to document what the local and indigenous people ate, drank, and used as medicine from the environment. He took

his young family, including Peggy, their two-and-a-half-year-old son John, and six-month-old daughter Celia, with him to Panama.

"It was extremely interesting, learning how closely these people were tied to the environment," Duke recalled.[10] He traveled by dugout canoe, and much of his work was conducted in the Darién province of Panama, a wilderness region that is considered to be one of the most dangerous in the world. (The Darién Gap is an approximately 60-mile stretch of wilderness that forms the only break in the 19,000-mile Pan-American Highway.) On one field trip in 1968, Duke and his colleague Joseph H. Kirkbride, Jr., PhD (now with the Smithsonian Institution's Department of Botany) hiked across Panama from Bocas del Toro province on the Atlantic side to Chiriquí province on the Pacific side. On another field trip, they hiked from Darién province to the Colombian border.

**Duke recognized the cultural and environmental problems that often occurred when developing countries clashed with developed countries. In 1970, still at Battelle Memorial Institute, he responded to a series of 10 articles alerting the scientific community that the Vietnam defoliation program (using Agent Orange) was having serious side effects in Vietnam.**

In Panama, Duke became immersed in what became his overriding professional interest: neotropical ethnobotany. During a collective four years of field work (between 1963 and 1970) in Panama and Colombia, he collected more than 15,000 specimens of plants, as well as amphibians, arthropods, birds, fish, mammals, and reptiles that were part of the food chain, especially of the Chocó (now Embera-Wounaan) and Cuna (now Guna) tribes.[18,19]

### Pondering "Progress" in Panama

Following his field collections, Duke spent several years in Columbus, Ohio, producing reports of his findings. His close connections with the people and environment in Panama added perspective to the debate over the plans for the controversial sea-level canal. In a letter to the editor of *Biological Conservation* he asked: "Where does Panama intend to deposit its solid wastes, treated or untreated? ... Where does Panama intend to put its thermal [nuclear] effluents? ... Any one of them if added in sufficient quantity at the centre of a sea-level canal, would be repugnant, if not lethal, to interoceanic migrants, including tourists. However, the sea-level canal was not proposed to accommodate tourists, but instead large ocean-going tankers."[20]

In another letter to the editor of *Science* he asked: "Does generosity of avarice dictate that the developed nations hinder the development of underdeveloped nations with environmental considerations? ... Progress is a magic word in Panama…. It is not politic to hinder progress; politicians usually decry pollution only when their constituents are crying pollution. Such is true in few, if any developing countries. Progress, *sí;* pollution control, *mañana*."[21] Duke's service was always to the people whose traditions he admired rather than the government entities or projects that employed him.

Duke recognized the cultural and environmental problems that often occurred when developing countries clashed with developed countries. In 1970, still at Battelle Memorial Institute, he responded to a series of 10 articles alerting the scientific community that the Vietnam defoliation program (using Agent Orange) was having serious side effects in Vietnam. Based on their experiences as tropical ecologists, Duke and his colleague John T. McGinnis sent a letter to the editor of *Science* recommending and outlining a practical 10-point research program on tropical reforestation that could "contribute to a successful rehabilitation of Vietnam to correct some of the side effects of the war." As an accomplished musician, poet, and songwriter, subtle humor would often creep into his scientific writings. The letter was titled "Vietnam Refoliation."[22]

With the completion of the voluminous feasibility studies on the proposed Atlantic-Pacific Interoceanic Canal, the five-member Canal Study Commission concluded, "Unfortunately, neither the technical feasibility nor the international acceptability of such an application of nuclear excavation technology has been established at this date."[23] And, surprising Duke, they also concluded that "The risk of adverse ecological consequences stemming from construction and operation of a sea-level Isthmian canal appears to be acceptable."

### From Drug Plants to Databases

Reading those conclusions, Duke raised an eyebrow, rubbed his chin, and returned to the Agricultural Research Service at the USDA in 1971 as chief of the Plant Taxonomy Laboratory, part of the Plant Genetics and Germplasm Institute. After the reorganization of the USDA's Agricultural Research Service in 1972, Duke's new assignment with the USDA, in conjunction with the United Nations, was to come up with alternative crops for narcotic plants. Viewing marijuana (*Cannabis* spp., Cannabaceae), coca (*Erythroxylum* spp., Erythroxylaceae), and poppies (*Papaver* spp., Papaveraceae) as economic plants, despite their legal status, he began compiling massive amounts of data on economic plants of the world. The data would not only serve as the foundation for his assigned program at the time, but would also become the foundational database for other programs that Duke directed. The list of projects including work on alternative agricultural crops, oilseed crops, alternative energy-related crops, and underutilized food

Above photo: Duke and *tonga de monte* or *I wua* (Chocó), a plant in the genus *Solanum* used as a narcotic and painkiller. The shrub is 1-2 m tall and has white flowers, purplish anthers, and orange berries. Tres Bocas on the Río Coasi, Darién, Panama, May 1968. Photo ©2018 Joseph H. Kirkbride, Jr.

crops. One of the most significant outcomes was the largest compilation of data on medicinal plants ever amassed by an individual.

By 1981, the computerized list of medicinal plants produced by Duke and colleagues at the Economic Botany Laboratory (formerly known as the Medicinal Plant Resources Laboratory) would include more than 85,000 entries.[24] This would become the heart of his groundbreaking "Phytochemical and Ethnobotanical Databases," which he updated from the 1970s until his retirement in 1995. The database is now permanently archived, and it is still available through the National Agricultural Library and remains one of the most frequently accessed USDA databases.[25‡]

Recognizing that a weed in one part of the world may be a food or fodder crop elsewhere, or that a medicinal plant in one country may be an illegal narcotic in another, Duke and his team generated a list of 1,000 lesser-known crop species and developed a matrix that included information about their "ecological amplitude" from one region to another. The data matrix included taxonomic, ecological, morphological, geographical, pathological, ethnobotanical, biochemical, and economic data that grew out of the crop diversification program. His "Crop Diversification Matrix" was published in 1974,[26] along with a paper on the ecological amplitudes of herbs, spices, and medicinal plants.[27]

The comparative data were collected from correspondents at agricultural stations and botanical gardens from around the world who provided information about economic plants that were successfully grown in their regions (without irrigation). Duke and his team complied annual precipitation data from each region, along with temperature, pH, and soil data. Later publications would also include data about nutritional values.[28,29]

The work also served the public interest. The Plant Genetics and Germplasm Institute held the largest taxonomic collection of seeds in the world, which served local, national, and international identification of seeds, and in several instances prevented deaths and solved the cause of

‡ Until several months before his passing, Duke continued his activities as an avid compiler of voluminous medicinal plant information into the successor databases, known as "Father Nature's Farmacy."

fatalities. Duke's lab also became a primary source for identifying fragmentary narcotic and poisonous plant material.[30]

## Poppy Pursuits

*Poppyseed rolls too hot or hardened*
*The seed will not grow in the garden;*
*But if the seeds are to germinate,*
*Narcotic laws are violated;*
*Poppy patches are not to be pardoned!*

—From *Herbalbum: An Anthology of Varicose Verse*[31]

In the early 1970s, Duke turned his professional attention to poppies. This work took him to various parts of the world, including Iran to collect opium poppy (*P. somniferum*) germplasm from the plant's center of genetic diversity, as well as to document opium production practices. In 1971, he observed poppy production among Meo ethnic minority villages in Thailand and a Yao village in Vang Vieng, Laos.[32]

Looking beyond the obvious abuse potential of opium poppy as a narcotic, Duke turned his attention to the plant group's broad economic potential. He wrote about poppy's potential as an ornamental and a source for poppy seed, poppy seed oil, high-protein poppy-cake, poppy flour, and poppy as a vegetable. He saw the potential for poppies to be used as a commercial ant feed, antimalarial, cough remedy, and salad vegetable, among other purposes.

He documented the adulteration of marijuana with opium, morphine, or codeine and speculated that this adulteration could have contributed to the perception of marijuana as a gateway to opiate abuse. He observed that where both marijuana and opiates were illegal, they were often sold in the same illicit channels, associating one with the other. He became an early advocate for the legalization of marijuana, believing this was the best way to control its economics and availability. He observed that tribal herbalists in India had both marijuana and opium in their medicine kits. How, he asked, can one eliminate opium and marijuana in populations where 80% of the people are attended by Ayurvedic or Unani-Tibb practitioners?[33] His detailed observations and information on the genus *Papaver* could be revisited for leads on to how to deal with the modern opioid crisis. Clues might be found in the *Annotated Bibliography on Opium and Oriental Poppies and Related Species*, a 1973 book with Duke as lead author.[34]

## Chief, USDA Medicinal Plant Resources Laboratory

In 1977, the USDA appointed Duke as chief of the Medicinal Plant Resources Laboratory, which was then renamed the Economic Botany Laboratory, apparently because of the controversies then emerging about herbal products in the early years of the natural food industry. From 1977 to 1981, Duke headed the USDA's collaboration with the National Cancer Institute (NCI) to collect plant specimens and promising biomass from all over the world that might have anticancer activities. This effort was inspired by the work of NCI scientist Jonathan L. Hartwell, PhD (1906-1991). Hartwell's pioneering work on the common mayapple (*Podophyllum peltatum*, Berberidaceae) resulted in the isolation of podophyllotoxin and several other compounds, which eventually led to the development of semisynthetic drugs used in chemotherapy for the treatment of testicular cancer and small cell lung cancer. In July 1960, a contract was established with NCI for the USDA to begin collections of plant materials for screening potential new anticancer compounds. Duke considered this his most important assignment during his service at the USDA, which took him to China, Egypt, South America, and elsewhere.

Between 1960 and 1980, the NCI screened approximately 35,000 species of higher (flowering) plants for activities against cancer. By 1977, approximately 3,000 of those had demonstrated reproducible activities. A small fraction of these, including mayapple, yew (*Taxus* spp., Taxaceae) derivatives, and others, were eventually chosen for clinical trials. Jonathan L. Hartwell's *Plants Used Against Cancer*, a compilation of 11 papers originally published in *Lloydia* (now the *Journal of Natural Products*) from 1967 to 1971 on folk cancer remedies worldwide, covered more than 3,000 species and includes more than 1,000 references.[35]

In 1981, the first year of Ronald Reagan's presidency, the NCI Natural Products Screening Program was removed from the federal budget. "I got a phone call," Duke recalled, "that the 25-year-old program, that wow, came to an abrupt and painful end."[36] At the time, Duke was in the process of bringing back 900 pounds of plant material from China, and his colleague, Richard W. Spjut, was bringing in more than a half-ton of plant material from Australia.

In Duke's foreword to the reprint of Hartwell's *Plants Used Against Cancer*, he lamented: "I view the publication as one epitaph to the cancer-screening program involving the National Cancer Institute with the U.S. Department of Agriculture for nearly 25 years. In a blow to natural-products chemistry in the United States, the Board of Scientific Counselors, Division of Cancer Treatment, National Cancer Institute, voted on October 2, 1981, to abolish the NCI research program concerned with the development of antitumor agents from plants. I fear this signals the end of significant government-sponsored research in the United States on medicinal plants, leaving research to the pharmaceutical firms, who have shown relative disinterest in plant products."[37]

After his appointment as chief of the USDA's Medicinal Plant Resources Laboratory in 1977, Duke garnered international notoriety for his work in economic botany and medicinal plants, as well as attention from the popular press. He was profiled in *People* magazine's April 4, 1977 issue, and became a fixture on the lecture circuit, speaking on medicinal plants and herbs at professional and public venues. He emerged as the public face of the federal government for all things herbal and carefully upheld a conservative approach to herb use as a government scientist. Jim Duke had to walk an uncomfortable tightrope between his personal beliefs advocating the use of herbs and at the same time emphasizing that he deferred "the prescribing of medicines" to medical professions, be they physicians or shamans.

## Academic and Popular Author

Duke kept one foot in academia and the other in popular interpretation of the use of herbs. He produced roughly an equal number of technical books and popular books on herbal topics. He was quick to publish in newsletters and magazines such as *Well-Being*, *Bu$iness of Herbs*, *Colt's Foot*, *Prevention*, *Mother Earth News*, and, of course, in *HerbalGram*.

Duke also published books and booklets, some of which were directly related to his USDA career. In 1972, he self-published a dictionary of colloquial slang terms in various Latin American language variations and dialects, and this was intended for diplomats and scientists working in the region.[38] Based on his earlier field work in Panama, he also published the *Isthmian Ethnobotanical Dictionary* in 1972,[39] a booklet that was later revised and published as a hardcover title by a publisher in India.[40]

With the end of USDA's contract with the NCI, a disappointed Duke became chief of the Germplasm Resources Laboratory at USDA, but he also pursued more of his own writings and activities.

In a 1988 interview, he mused: "Feeling sorry for me, USDA let me take the momentum I had gotten in medicinal plants to go off duty and publish what has been a best-seller for CRC Press (in CRC terms), *The Handbook of Medicinal Herbs*, and that one came out in 1985.[36]



Selections of the collected professional and popular books by James A. Duke. Photo ©2018 Steven Foster

"The USDA has no medicinal plant program since that moment in 1981 when the cancer program was terminated," he recalled in the same interview.[36] "And I have a feeling this is appropriate. The USDA is into food, fiber, and fodder, and even our country is not much into medicinal plants. Why should an agency of our country be into medicinal plants? … I'm not saying this is my philosophy. I believe in medicinal plants, but the USDA really should not have much involvement in medicinal plants. So, I sort of hung myself there, didn't I?" He laughed.

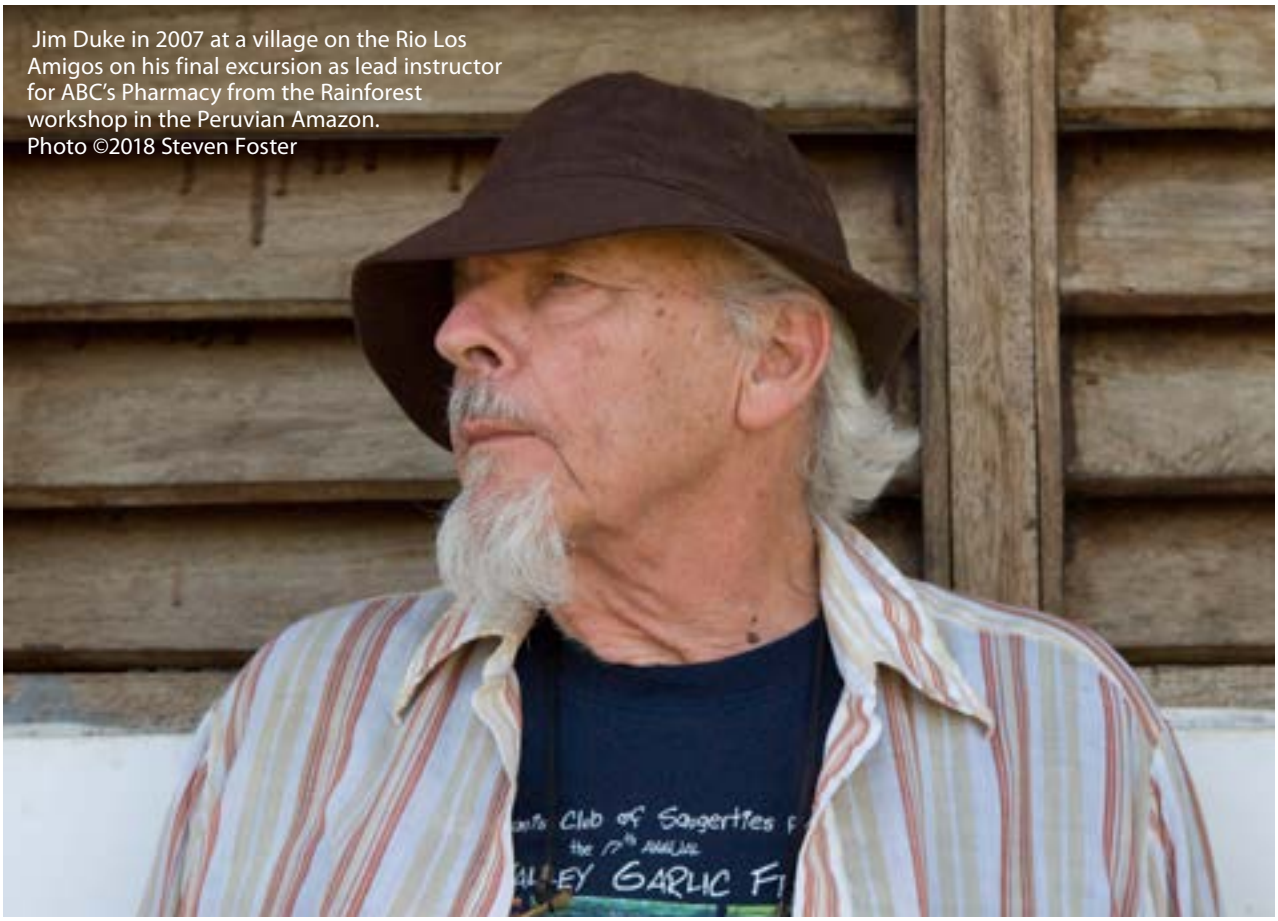
Duke looked ahead to "retirement" so he could get to work. In a letter to this author dated June 12, 1986, he predicted: "I may have to retire to the ginseng patch at 57. That'll give me 10 good but lean years of trying to turn the U.S. away from the synthetics to the natural. Quite an unholy and unlikely crusade."[41] Retirement was not to come as quickly as he thought. Duke persisted at the USDA for another nine years before retiring at age 66.

Although his books started with massive USDA data-collection projects, he was allowed to continue to work with his USDA files to shape them into reference books. From 1981 until his retirement in 1995, the USDA permitted him to continue his medicinal plant research "off duty."[36]

The majority of Duke's book-publishing activity occurred after the USDA's collection activities for the NCI ceased in 1981. His first professional title, *Handbook of Legumes of World Economic Importance* (Plenum Press, 1981), was based on data he collected about alternative crops and was a detailed survey of 140 species of legumes.[42] In 1983, the first of three editions from three separate publishers of *Medicinal Plants of the Bible* was issued.[43-45] In 1985, he co-authored (with Edward S. Ayensu) a two-volume work titled *Medicinal Plants of China* (Reference Publications), which featured an introductory chapter that compared North American and Chinese medicinal plants.[46]

Duke's herbal publishing leaped from academia to literary humor with the self-published, staple-bound, rare *Herbalbum: An Anthology of Varicose Verse* (1985), which included more than 500 herbal poems — doggerels and limericks — along with a collection of bluegrass songs and their simplified notated melodies and chords. In 1986, the songs were cut into a LP vinyl record with studio bluegrass musicians, recorded in Nashville, and titled *Dr. James A. Duke Presents The HerbAlbum*.

In quick succession, he completed small press popular books, including a book on growing and using culinary herbs[47]; the *Handbook of Northeastern Indian Medicinal Plants* (Quarterman Publications, 1986)[48]; *Living Liqueurs* (Quarterman Publications, 1987), a practical approach to having your herb and drinking it too, with the aid of cheap vodka[49]; and *Ginseng: A Concise Handbook* (Reference Publications, 1989).[50] In 1990, he coauthored *Peterson Field Guide to Medicinal Plants and Herbs of Eastern and Central America* (with this author, S. Foster) in Houghton Mifflin Harcourt's Peterson Field Guide series, with a second edition in 2000 and a third edition in 2014.




Jim Duke in 2007 at a village on the Rio Los Amigos on his final excursion as lead instructor for ABC's Pharmacy from the Rainforest workshop in the Peruvian Amazon. Photo ©2018 Steven Foster

### Academic Publishing Success

The success of his 1985 *CRC Handbook of Medicinal Herbs*, which included 365 herbs, or an herb a day, a constant Duke mantra, led to the publication of at least a dozen more CRC titles, including academically obscure tabular compilations such as the *CRC Handbook of Proximate Analysis Tables of Higher Plants* with A.A. Atchley (1986) and the four-volume *CRC Handbook of Agricultural Energy Potential of Developing Countries* with A.A. Atchley, K. Ackerson, and P. Duke. Technically rich but readable books for knowledgeable enthusiasts include the *CRC Handbook of Nuts* (1989), *CRC Handbook of Edible Weeds* (1992), *CRC Handbook of Alternative Cash Crops* with J.L. duCellier (1993), and *Duke's Handbook of Medicinal Plants of Latin America* with M.J. Bogenschutz-Godwin and A.R. Ottesen (2009). His CRC titles became an academic publishing franchise.

### Birth of a Bestseller

In a letter dated June 26, 1995, Duke wrote to this author: "For better or worse, for me, for herbal industry, for Rodale, for USDA, I have signed a contract with Rodale to do, in one year, yet another book on herbal medicine. There are already too many. And I am not as optimistic about this one as they are. And the one year deadline forces me to retire on Sep. 30 [1995] to devote near full time to Rodale (except for an ecotour here and there, like joining you in the Amazon in October for example)."[51]

A year later, he was finishing the final draft of his book *The Green Pharmacy*, published by Rodale in 1997. It was to become a runaway bestseller with more than a million copies sold, and then spun-off into additional Rodale book titles including *Dr. Duke's Essential Herbs* (1999), *The Green Pharmacy: Anti-Aging Prescriptions* with Michael Castleman (2001), and *The Green Pharmacy: Guide to Healing Foods* (2008), among others. *The Green Pharmacy* was one of the best-selling herbal title franchises of all time.

The Dukes purchased a six-acre farmette in Fulton, Maryland, in 1971, about 16 miles from the USDA's Agricultural Research Service campus in Beltsville, Maryland. The Dukes christened the farm "Herbal Vineyard." It was here that Duke "retired" and created a four-acre herb garden with hundreds of plant species, in plots arranged by medical conditions, following the chapters in *The Green Pharmacy*. Thousands of people have visited and been inspired by the rural Maryland garden, and countless individuals were introduced to the botanical diversity of the tropics through Jim's leading more than 60 tours to the Amazon, Costa Rica, and elsewhere during his productive retirement years. Many of these tours happened via the American Botanical Council's "Pharmacy from the Rainforest" ethnobotany ecotours, which were continuing education approved for pharmacists and other health professionals.

Steven Foster and Jim Duke in the Arkansas Ozarks in May 1992. Photo ©2018 Steven Foster

**Many times I had a research question while working in his basement library, to which Jim had the answer, not always on his computer, but by walking to a bookshelf and opening some tome or other to the precise page that held the information in question. His erudition and deep earthy wisdom was even more comprehensive than his library. He lived his love of plants. His enormous legacy includes his living gardens, to be cared for and maintained as a premier teaching classroom by Maryland University of Integrative Health. Beyond MUIH and around the planet we celebrate James A. Duke through song, stories of his humor, brilliance and inspiring humanity.**

– Amanda McQuade Crawford

## Remember This

Jane P. Gates, of the Alternative Farming Systems Information Center at the USDA National Agricultural Library, asked Duke in a 1988 interview, "What would you like to be remembered for?"[52] Standing barefoot in his garden with his signature plaid shorts, Duke replied:

> Something I haven't done yet. I would like to be remembered for turning around the trend to the natural medicine from the synthetic medicine. I think we made a mistake there, because through evolution, my genes and immune system have already experienced all of the poisons that are here in this garden, or many of them, because my grandparent's grandparents ate or used these things for one thing or another, such that my genes have already touched those poisons, my genes have not experienced tomorrow's synthetics. Two hundred years ago, all of our medicines were natural. Today, still, 25% of prescription drugs are based on higher plants and almost half of our prescription drugs are based on lower plants, higher plants, and animals, so even today 50%, or almost 50%, are natural. So, I would like to see that [we] go back to 100% natural. I really believe that natural is safer than the synthetics. HG

***Steven Foster*** *is an author, photographer, and herbalist, and he serves on the Board of Trustees of the American Botanical Council. His most recent book is the third edition of the* Peterson Field Guide to Medicinal Plants and Herbs of Eastern and Central North America *(Houghton Mifflin Harcourt, 2014), which he co-authored with James A. Duke, PhD.*

## References

1. Miller S, Morehouse M. Jungle Jim: To botanist Jim Duke herbal healing is no fad—it's the best medicine. *People.* February 1, 1999:113-117.
2. Gates JP. Part 1. Introduction and early life. Oral history interview with Dr. James A. Duke. Beltsville, MD: US Department of Agriculture, National Agricultural Library, Alternative Farming Systems Information Center, Videocassette No. 629, 1988. Available at: www.nal.usda.gov/afsic/james-duke.
3. Gates JP. Part 2. Early botanical interests and early memories. Oral history interview with Dr. James A. Duke. Beltsville, MD: U.S. Department of Agriculture, National Agricultural Library, Alternative Farming Systems Information Center, Videocassette No. 629, 1988. Available at: www.nal.usda.gov/afsic/james-duke.
4. Duke JA. Letter to Mrs. Hillary Rodham Clinton, April 5, 1993.
5. Gates JP. Part 3. Early botanical interests and early memories. Oral history interview with Dr. James A. Duke. Beltsville, MD: US Department of Agriculture, National Agricultural Library, Alternative Farming Systems Information Center, Videocassette No. 629, 1988. Available at: www.nal.usda.gov/afsic/james-duke.
6. Anon. *Billboard.* August 23, 1947:118.
7. Warlick T, Warlick L. *The WBT Briarhoppers*: *Eight Decades of a Bluegrass Band Made for Radio*. Jefferson, NC: MacFarland & Company, Inc.; 2007.
8. Gates JP. Part 4. College, military service and post graduate work. Oral history interview with Dr. James A. Duke. Beltsville, MD: US Department of Agriculture, National Agricultural Library, Alternative Farming Systems Information Center, Videocassette No. 629, 1988. Available at: www.nal.usda.gov/afsic/james-duke.
9. Radford RE, Ahles HE, Bell CR. *Manual of the Vascular Flora of the Carolinas.* Chapel Hill, NC: University of North Carolina Press; 1968.
10. Gates JP. Part 5. Work in the botany of Latin America. Oral history interview with Dr. James A. Duke. Beltsville, MD: US Department of Agriculture, National Agricultural Library, Alternative Farming Systems Information Center, Videocassette No. 629, 1988. Available at: www.nal.usda.gov/afsic/james-duke.
11. Dwyer JD. Notes on the Lecythidaceae of Panama. *Ann Mo Bot Gard.* 1965;52(3):351:363.
12. King RM, Robinson H. Studies in the Eupatorieae (Asteraceae) CXX. Additions to the Genus *Koanophyllon* in Panama. *Phytologia.* 1974;28(1):67-72.
13. Dwyer JD. Rubiaceae. In: Woodson RE, Schery RW. Flora of Panama, Part IX. *Ann Mo Bot Gard.* 1980;67:371.
14. Dwyer JD, Hayden SMV. Notes on woody Rubiaceae of tropical America. *Ann Mo Bot Gard.* 1967;54:138-146.
15. Dwyer JD. Dukea. A new genus of the Rubiaceae (Tribe Mussaendeae). *Ann Mo Bot Gard.* 1966;53(3):360-367.
16. Duke JA. Keys for the identification of seedlings of some prominent woody species in eight forest types in Puerto Rico. *Ann Mo Bot Gard.* 1965;52(3):324-350.
17. Duke JA. Darienita's Dietary. Bioenvironmental and radiological-safety feasibility studies, Atlantic-Pacific Interoceanic Canal, 112 pp., 1970. Abstract 202 in Environmental Plutonium Data Base Group, Environmental Sciences Division, eds. *Environmental Aspects of Plutonium and Other Elements. A Selected, Annotated Bibliography.* Oak Ridge, TN: US Atomic Energy Commission. ORNL-EIS-73-21 (Suppl. 1):200 August, 1973.]
18. Duke JA. Ethnobotanical observations on the Choco Indians. *Econ Bot.* 1970;24(3):344-366.
19. Duke JA. Ethnobotanical observation on the Cuna Indians. *Econ Bot.* 1975;29(3):278-293.
20. Duke JA. The sea-level canal accord? *Biological Conservation*. 1971;4(1):17.
21. Duke JA. Aquatic ecosystems. *Science*. 1972;176:582.
22. Duke JD, McGinnis, JT. Vietnam refoliation. *Science*. 1970;107:807.
23. Atlantic-Pacific Interoceanic Canal Study Commission, eds. *Interoceanic Canal Studies.* Washington, DC. 1970.
24. Duke JA, Wain KK. Medicinal plants of the world. Computer index with more than 85,000 entries. 1981 (unpublished).
25. Dr. Duke's Phytochemical and Ethnobotanical Databases. National Agricultural Library, US Department of Agriculture website. Available at: https://phytochem.nal.usda.gov/phytochem/search. Accessed January 24, 2018.
26. Duke JA, Terrell EE. Crop Diversification Matrix: Introduction. *Taxon*. 1974;23(5/6):759-799.
27. Duke JA, Hurst SJ. Ecological amplitudes of herbs, spices and medicinal plants. *Lloydia*. 1975;38(5):404-410.
28. Duke JA. Vegetarian vitachart. *Quart J Crude Drug Res.* 1977;15:45-66.
29. Duke JA. Nutritional values for crop diversification matrix. *Ecol. Food and Nutrition*. 1977;6:39-48.
30. Duke JA, Moseman JG. Papaveraceous Polyclave. *Critical Reviews in Toxicology*. 1974;3(1):1-95.
31. Duke JA. *Herbalbum: An Anthology of Varicose Verse*. JA Duke: Fulton, MD; 1985.

32. Duke JA. Notes on Meo and Yao poppy cultivation. *Phytologia*. 1974;28(1):5-8.
33. Duke JA. Utilization of *Papaver*. *Econ Bot*. 1973;27(4):390-400.
34. Duke JA, Gunn CR, Leppik EE, Reed CF, Solt ML, Terrell EE. *Annotated Bibliography on Opium and Oriental Poppies and Related Species*. Beltsville, MD: Agricultural Research Service, US Department of Agriculture. ARS-NE 28; December, 1973.
35. Hartwell JA. *Plants Used Against Cancer: A Survey.* Lincoln, MA: Quarterman Publications, Inc.; 1982.
36. Gates JP. Part 6. Medicinal plants and publications. Oral history interview with Dr. James A. Duke. Beltsville, MD: US Department of Agriculture, National Agricultural Library, Alternative Farming Systems Information Center, Videocassette No. 629, 1988. Available at: www.nal.usda.gov/afsic/james-duke
37. Duke JA. Foreword. In: Hartwell J. *Plants Used Against Cancer: A Survey*. Lincoln, MA: Quarterman Publications, Inc.; 1982:v-vii.
38. Duke JA. *Lewd Latin Lexicon*. Fulton, MD: JA Duke; 1972.
39. Duke JA. *Isthmian Ethnobotanical Dictionary*. Fulton, MD: JA Duke; 1972.
40. Duke JA. *Isthmian Ethnobotanical Dictionary*. 3rd ed. Johdpur, India: Scientific Publishers; 1986.
41. Duke JA. Letter to Steven Foster. June 12, 1986.
42. Duke JA. *Handbook of Legumes of World Economic Importance*. New York, NY: Plenum Press; 1981.
43. Duke JA. *Medicinal Plants of the Bible*. New York, NY: Conch Publications; 1983.
44. Duke JA. *Herbs of the Bible*: *2000 Years of Plant Medicine*. Loveland, CO: Interweaver Press; 1999.
45. Duke JA, Duke PAK, duCellier, JL. *Duke's Handbook of Medicinal Plants of the Bible*. Boca Raton, FL: CRC Press; 2008.
46. Duke JA, Ayensu ES. *Medicinal Plants of China*. 2 vols. Algonac, MI: Reference Publications; 1985.
47. Duke JA. *Culinary Herbs: A Potpourri.* New York, NY: Trado-Medic Books; 1985.
48. Duke JA *Handbook of Northeastern Indian Medicinal Plants.* Lincoln, MA: Quarterman Publications; 1986.
49. Duke JA. *Living Liqueurs.* Lincoln, MA: Quarterman Publications, Inc.; 1987.
50. Duke JA. *Ginseng: A Concise Handbook.* Algonac, MI: Reference Publications; 1989.
51. Duke JA. Letter to Steven Foster, June 26, 1995.
52. Gates JP. Part 9. Farming practices, evening primrose, thoughts on the future. Oral history interview with Dr. James A. Duke. Beltsville, MD: US Department of Agriculture, National Agricultural Library, Alternative Farming Systems Information Center, Videocassette No. 629, 1988. Available at: www.nal.usda.gov/afsic/james-duke.


Amanda McQuade Crawford and Jim Duke stroll back to camp at sunset along the Amazon in November 1995.
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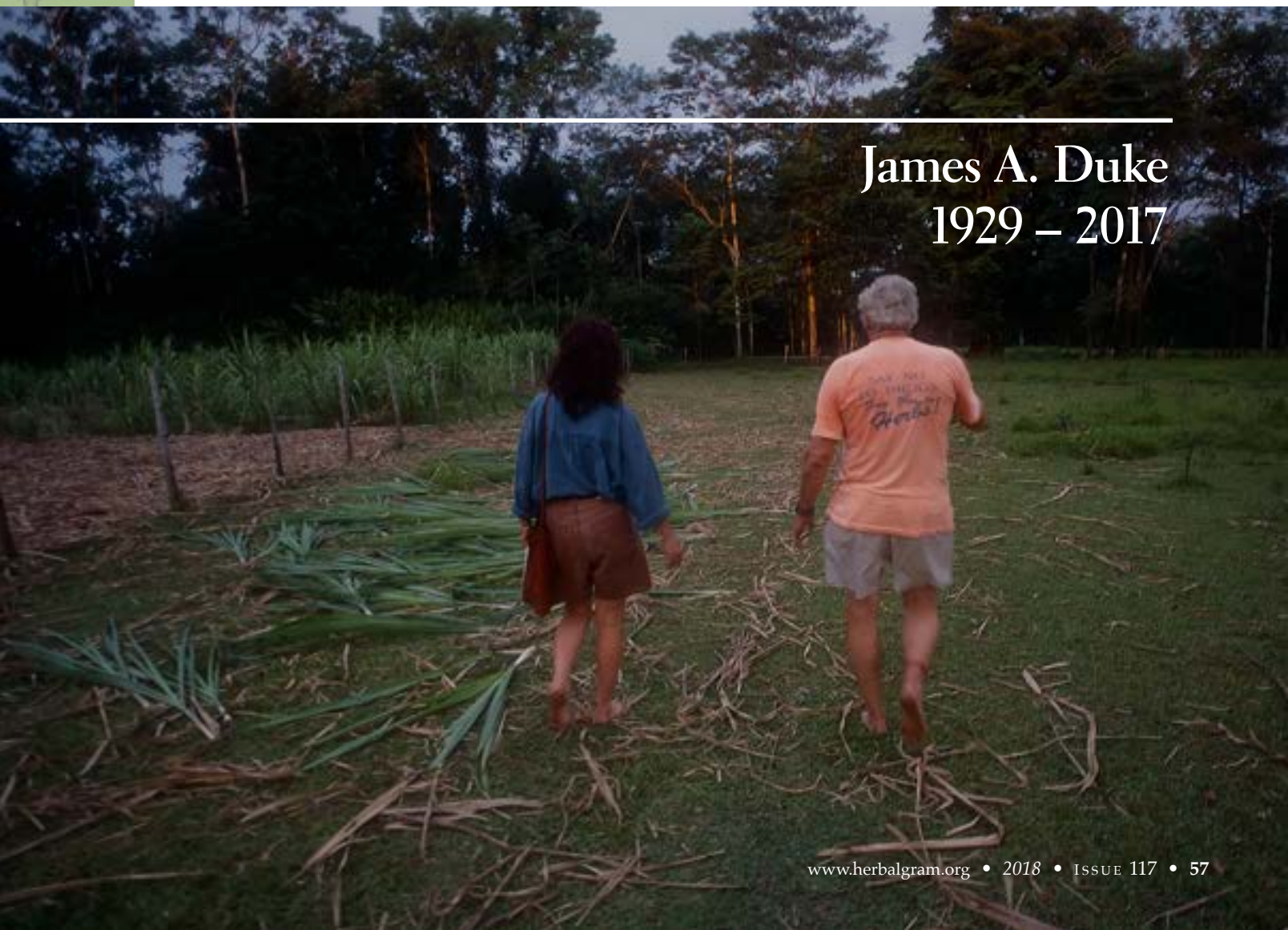
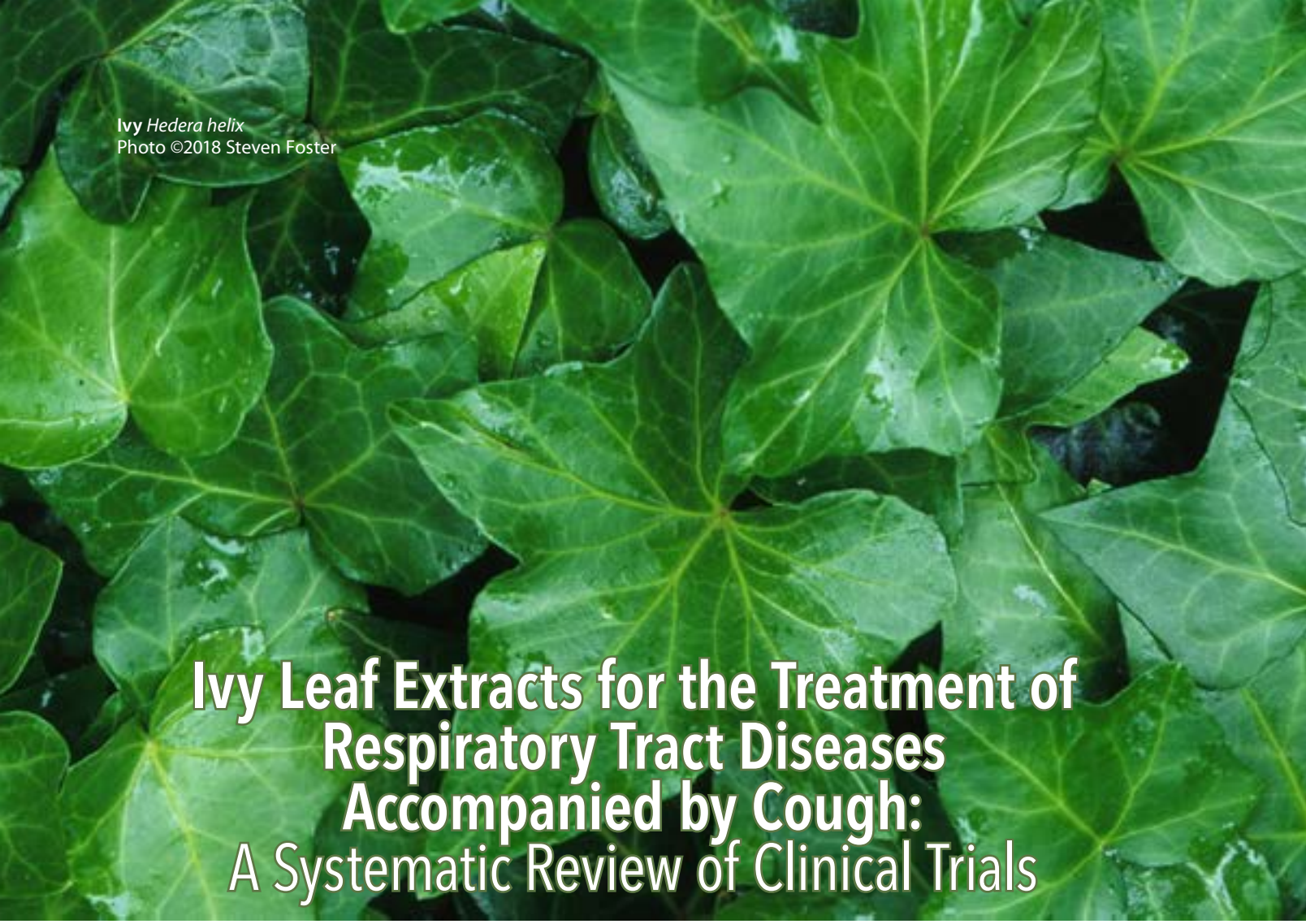


# James A. Duke
# 1929 – 2017



**Ivy** *Hedera helix*
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# Ivy Leaf Extracts for the Treatment of Respiratory Tract Diseases Accompanied by Cough: A Systematic Review of Clinical Trials

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## Summary

Ivy (*Hedera helix*, Araliaceae) leaf extracts have long been used to treat respiratory diseases, and they are widely accepted by patients and health care providers for this purpose. This systematic literature review evaluates clinical data on the efficacy and safety of ivy leaf extracts in different dosage forms for the therapy of respiratory diseases accompanied by cough. Nineteen clinical studies are evaluated. Among these are eight randomized clinical trials, two non-randomized controlled studies, and nine observational studies. Just one of the 19 reviewed studies was performed in a randomized, placebo-controlled, and double-blind design and fulfilled current criteria for randomized controlled trials (RCTs). The reviewed data indicate that ivy leaf extracts have a secretolytic effect in acute cough, although their efficacy for the treatment of chronic respiratory diseases is inconclusive. Adverse events (AEs) were rare and mostly related to gastrointestinal disorders or allergic reactions. No serious AEs were described.

## Background

Ivy is a vine that can climb to 20 meters (66 feet) with evergreen and dimorphic leaves. On non-flowering branches, the leaves have three to five lobes with white, fan-like venation, whereas on flowering branches, they are rhombic or lanceolate.[1] The taste and mouthfeel of the dried leaf have been described as bitter and raspy, respectively.[2]

Ivy leaves contain constituents such as flavonoid glycosides, phenolic acids, polyacetylenes, and saponins.[3] In vitro studies indicate that the monodesmosidic (a term that describes a molecule with a single glycoside chain) saponin α-hederin, which can emerge from the bisdesmosidic saponin hederacoside C during the drying process,[2] contributes to the overall pharmacological activity of ivy leaf extracts.[4-6] The underlying mechanisms are not yet fully understood, but pharmacological data suggest an increase

in the $\beta_2$-adrenergic responsiveness of alveolar type II cells and bronchial muscle cells may lead to the secretolytic and bronchospasmolytic effects observed in clinical studies.[7]

Clinical data have been obtained with various ivy extracts. Extracts with different drug extract ratios (DERs; see Table 1 for a full list of abbreviations used in this article) and/or different extraction solvents should be considered distinct active ingredients in herbal medicinal products, and results obtained in studies with distinct extracts are generally not interchangeable. Despite the available evidence on the pharmacological activities of α-hederin, neither standardization nor quantification of the α-hederin content in ivy leaf extracts has been performed so far. In addition, other detailed information on the composition of extracts used in clinical studies has not been reported. This also applies to the extracts used in pharmacological studies.

As a result of its anatomy, the respiratory tract in particular is exposed to a multitude of infectious, chemical, and physical sources of irritation. Thus, respiratory tract diseases are common. Acute and chronic forms of cough as a symptom of respiratory tract diseases can be distinguished. The common cold is a viral infection of the upper respiratory tract and the most frequent cause of acute cough. In about two-thirds of cases, this disease is self-limiting within two weeks. Acute bronchitis (AB) is accompanied by dry and, later, productive cough, and often fever, sore throat, and rhinitis.[8] Cough is considered to be productive (i.e., wet, with phlegm) if the amount of daily expectoration is at least 30 mL.[9]

To characterize respiratory diseases, the analysis of lung function via spirometry is a widely used method. Spirometry involves the recording and interpretation of a flow-volume curve and provides information about vital capacity (VC), forced vital capacity (FVC), forced expiratory volume (FEV) in one second ($FEV_1$), and maximal expiratory flow (MEF) of the lungs. The explanatory power of this diagnostic method depends on patient cooperation and the qualification of the examiner.[10] Therefore, researchers may choose to use additional analytical techniques. Body plethysmography, for example, can provide information about functional residual capacity (FRC), specific airway resistance ($sR_{AW}$), lung residual volume (RV), total lung capacity (TLC), intrathoracic gas volume (ITGV), and airway resistance ($R_{AW}$).[11]

Although time thresholds can overlap, chronic cough is defined as a cough that persists for longer than eight weeks.[8] Asthma is a chronic inflammatory airway obstruction that is reversible (in contrast to chronic obstructive pulmonary disease [COPD], which is considered irreversible) and accompanied by bronchial hyper-reactivity. Differentiating between asthma and COPD is clinically relevant, especially in adults, since symptoms may overlap but treatment options differ. A bronchodilation test is an essential diagnostic tool that describes the reversibility of airway obstructions. To this end, $FEV_1$ is measured before and after inhalation of a short-acting ß-sympathomimetic bronchodilator. Asthma is characterized by a change in $FEV_1$ ($\Delta FEV_1$) that is greater than 15%, whereas COPD presents as a $\Delta FEV_1$ of less than 15%. The course of disease is episodic for asthma and progredient (i.e., progressive) in the case of COPD. Moreover, COPD can be accompanied by pulmonary emphysema. Peak expiratory flow (PEF) can be monitored with a peak flow meter for the evaluation of therapy success and progression control of respiratory diseases, especially in asthma.[12,13]

Expectorants are a valuable therapeutic option in acute and chronic respiratory diseases. In this context, herbal remedies have a long and well-documented tradition of use. Single-chemical entities, such as ambroxol and acetylcysteine (ACC), are also commonly used expectorants. Several European Union (EU) countries have authorized herbal medicinal products that contain ivy leaf extracts based on their well-established medicinal use as an expectorant in cases of productive cough.[14]

This review will evaluate the clinical data on the efficacy and safety of ivy leaf extracts for the therapy of respiratory diseases accompanied by cough.

**Table 1. Abbreviations Used in This Article**

| | |
|---|---|
| AB | Acute bronchitis |
| ACC | Acetylcysteine |
| ACQ | Asthma Control Questionnaire |
| AE | Adverse event |
| BSS | Bronchitis severity scale |
| CGI | Clinical global impression scale |
| COPD | Chronic obstructive pulmonary disease |
| DER | Drug extract ratio |
| FEV | Forced expiratory volume |
| $FEV_1$ | Forced expiratory volume in one second |
| FRC | Functional residual capacity |
| FVC | Forced vital capacity |
| GEA | Global efficacy assessment |
| HMPC | Committee on Herbal Medicinal Products |
| ITGV | Intrathoracic gas volume |
| ITT | Intention to treat |
| MEF | Maximal expiratory flow |
| MID | Minimal important difference |
| PAQLQ | Pediatric Asthma Quality of Life Questionnaire |
| PEF | Peak expiratory flow |
| PP | Per protocol |
| $R_{AW}$ | Airway resistance |
| RCT | Randomized controlled trial |
| RV | Residual volume |
| $sR_{AW}$ | Specific airway resistance |
| TLC | Total lung capacity |
| VAS | Visual analogue scale |
| VC | Vital capacity |
| VCD | Verbal category descriptive |

## Methods

### *Systematic Literature Search*

The MEDLINE (via PubMed) and Embase (via STN International) databases were searched in October 2016 for primary scien-

tific literature with a focus on clinical data assessing the safety and efficacy of ivy preparations as an expectorant in cases of productive cough. Since the Committee on Herbal Medicinal Products (HMPC) published a final EU herbal monograph[14] and an assessment report[15] on *H. helix* leaf in 2015, the retrieval period covered the gap between the last assessment of literature cited in the assessment report and the retrieval date (i.e., 2012-2016). To ensure completeness of the retrieval, a systematic approach was chosen that combined keyword searches (in the title and abstract) with the US National Library of Medicine's Medical Subject Headings, a controlled thesaurus of medical vocabulary. Search terms were as follows: hedera, ivy, Efeu, cough, respiratory tract diseases, respiratory mucosa, signs and symptoms respiratory. These terms were further connected with logical operators according to the PICO Model (a set of guidelines for clinical questions) in order to increase precision of the records found.

Overall, 204 records were retrieved from MEDLINE. The Cochrane Highly Sensitive Search Strategy, which was used to identify randomized clinical trials in MEDLINE, retrieved 13 RCTs from the 204 records. The Embase search was conducted in the basic index mode, which contains single words from the title, abstract, controlled terms, chemical name, and corporate (manufacturer) name, as well as Chemical Abstracts Service Registry Numbers. Different spellings were taken into account by setting the commands accordingly. A total of 66 citations were retrieved from Embase for the period from 2012 to 2016, applying a search strategy similar to the one used in MEDLINE.

Furthermore, several clinical trial registries were screened: ClinicalTrials.gov (a registry of clinical trials in the United States); EU Clinical Trials Register; PharmNet.Bund; and International Clinical Trials Registry Platform. In addition, the following clinical practice guidelines were reviewed: Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften e.V. (the Association of the Scientific Medical Societies in Germany), Nationale Versorgungsleitlinien, Evidence-Based Medicine Guidelines, and the guidelines developed by the World Health Organization. Overall, 75 records were retrieved from these sources.

All databases were searched irrespective of language and publication status, and no limitations on document types were set. A manual search by checking the reference lists of the retrieved articles and the use of standard textbooks completed the search procedure for relevant documents and information. All references were retrieved in a citation management tool and, after a duplicate check, a total of 369 citations were retrieved.

### *Literature Screening*

All retrieved publications were screened for inclusion criteria. Therefore, titles and abstracts were searched for the use of ivy as an intervention and the indication of respiratory disease in a clinical setting. Studies that did not meet these criteria were excluded. All full texts of the included studies were screened for valuable information corresponding to the addressed question. Here, only German or English full texts could be evaluated. The full texts of two clinical studies were not available[16,17] and, therefore, could not be considered in this review. Moreover, reviews and two studies with only historical meaning were excluded.[18,19] Ultimately, 19 clinical studies were evaluated in the context of this review.

**Table 2. Evidence Level Classifications of Clinical Studies***

| Evidence Level | Type of Study |
|---|---|
| Ia | Systematic review/meta-analysis of RCTs or "megatrial" |
| Ib | RCTs |
| IIa | Controlled cohort study (not randomized), controlled study, quasi-experimental study |
| IIb | Case-control study |
| III | Cross-sectional, ecological, or observational study, case series |
| IV | Expert opinion, basic research |

* Adapted from DEGAM (2014)[8]

### *Data Analysis and Quality Assessment*

All reviewed studies were classified according to their study design in terms of evidence levels (Table 2). Controlled studies were further categorized depending on the kind of study control (placebo, active comparator, or other ivy leaf extract formulations). The quality of included studies was assessed using methodological checklists created by the Scottish Intercollegiate Guidelines Network.[20] These checklists address questions about the study design, procedure with and number of dropouts, validity of outcome measurements, and statistical power. A summary of study specifics can be found in Table 3.

## Results

### *Placebo-controlled Studies*

In 2016, Schaefer et al.[21] conducted a randomized, placebo-controlled, double-blind, multicenter clinical study that assessed the efficacy and safety of ivy leaf extract for the treatment of acute cough in adults. The researchers used the cough liquid formulation Prospan Hustenliquid (Engelhard Arzneimittel GmbH & Co. KG; Niederdorfelden, Germany), which is characterized by a DER of 5-7.5:1 using a 30% (m/m) ethanol extraction solvent. A total of 181 patients (18-75 years of age) across five sites were included, and 178 patients completed the trial. Daily drug dose was 105 mg of ivy leaf extract over a treatment period of seven days, whereas the control group received what the authors described as an "inactive, adequate placebo." The primary outcome variable was cough severity assessed via visual analogue scale (VAS) over the whole treatment period of seven days, at the end of the seven-day treatment period, and at the end of the one-week observation period (day 14). Cough severity was also assessed by the bronchitis severity scale (BSS) and the verbal category descriptive (VCD) scale over the whole treatment period of seven days, as well as a global efficacy assessment (GEA) on days seven and 14.

## Table 3. Overview of Reviewed Clinical Studies on Ivy Leaf Extracts

| Evidence Level* | Authors | Objective | Subjects | Dropouts | Age Range | Study Sites | Formulation | DER and Extraction Solvent | Daily Dose (Ivy Leaf Extract) | Control | Treatment Period | Concomitant Drug Intake | Outcome Measures |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Ib | Schaefer et al. 2016 | Acute cough | 181 | 3 | 18-75 | 5 | Liquid | 5-7.5 : 1 ethanol 30% (m/m) | 105 mg | Placebo | 7 days | No | Cough severity by VAS, BSS, VCD, AE documentation |
| Ib | Zeil et al. 2014 | Asthma | 30 | 1 (+ 5 with low compliance) | 6-12 | 1 | Syrup | 5-7.5 : 1 ethanol 30% (m/m) | 70 mg | Placebo | 28-30 days | Yes | $MEF_{75-25}$, $FEV_1$, $R_{AW}$, TLC, VC, FVC, RV, FRC, $MEF_{50}$, $MEF_{25}$, FeNO, exhaled breath condensate pH, peak flow profile, PAQLQ, ACQ |
| Ib | Cwientzek et al. 2011 | Acute bronchitis | 590 | 72 | 2-86 | 7 | Drops | 2.2-2.9 : 1 ethanol 50% (v/v) : propylene glycol (98 : 2) | Treatment: N/A Comparator: 25.2 mg (2-4 y) 33.6 mg (4-10 y) 50.4 mg (> 10 y) | Ivy cough drops DER 5-7.5 : 1 ethanol 30% (m/m) | 7 days | Yes | Cough severity by BSS, VAS, AE documentation |
| Ib | Unkauf/ Friedrich 2000 | Dry and painful or productive cough | 52 | 0 | 0-12 | N/A "multicenter" | Syrup | 3-6 : 1 ethanol 60% (v/v) | N/A | Ivy cough syrup DER 5-7.5 : 1 ethanol 30% (m/m) | 10 days | N/A | VAS, clinical global impression, characterization of cough and auscultation, AE documentation, lab analysis |
| Ib | Mansfeld et al. 1998 | Asthma | 28 | 4 | 4-12 | 1 | Drops | 5-7.5 : 1 ethanol 30% (m/m) | 35 mg | Placebo | 3 days | No | $R_{AW}$, ITGV, RV, VC, FVC, $FEV_1$ |
| Ib | Mansfeld et al. 1997 | Chronic obstructive respiratory disease | 26 | N/A | 5-11 | 1 | Suppositories | 5-7.5 : 1 ethanol 30% (m/m) | 160 mg (suppositories) 35 mg (drops) | Ivy cough drops | 3 days | Yes | $FEV_1$, FVC, PEF, $R_{AW}$, ITGV, RV, $sR_{AW}$ |
| Ib | Gulyas et al. 1997 | Chronic obstructive respiratory disease | 27 | 2 | 10-15 | N/A | Syrup | 5-7.5 : 1 ethanol 30% (m/m) | 105 mg (syrup) 42 mg (drops) | Ivy cough drops | 10 days | N/A | $FEV_1$, FVC, VC, PEF, $R_{AW}$, ITGV, $sR_{AW}$ |
| Ib | Meyer-Wegener et al. 1993 | Chronic bronchitis | 99 | 1 | 25-70 | 1 | Drops | 5-7.5 : 1 ethanol 30% (m/m) | 42-70 mg | Ambroxol tablets | 4 weeks | No | VC, FVC, $FEV_1$, peak flow profile, auscultation, diary |
| IIa | Bolbot et al. 2004 | Acute bronchitis | 50 | N/A | 2-10 | 2 | Undeclared formulation | 5-7.5 : 1 ethanol 30% (m/m) | 105 mg (2-6 y) 210 mg (7-10 y) | Acetylcysteine | 7-10 days | Yes | Cough and sputum characterization, short breath, respiratory pain, FVC, $FEV_1$, PEF, $MEF_{25}$, $MEF_{50}$, $MEF_{75}$, $AWSV_{25-75}$ |
| IIa | Maidannik et al. 2003 | Acute and chronic respiratory diseases | 72 | N/A | 0-15 | 2 | Syrup | 5-7.5 : 1 ethanol 30% (m/m) | 3 teaspoons (1-6 y) 6 teaspoons (7-14 y) | Ambroxol syrup | Acute: 7-10 days Chronic: 10-14 days | Yes | Verbal rating on efficacy, characterization of cough, auscultation, external respiration, short breath, leukocyte count |
| III | Schmidt et al. 2012 | Acute respiratory catarrh and/or chronic recidivating inflammatory bronchial disease | 272 | 15 | 0-13 | 14 | Syrup and drops | 2.2-2.9 : 1 ethanol 50% (v/v) : propylene glycol (98 : 2) | 50 mg (0-1 y) 150 mg (1-4 y) 200 mg (4-10 y) 300 mg (10-13 y) | N/A | Average: 10 days | No | Verbal rating of severity and development of clinical symptoms, tolerability, compliance, taste, ease of application, AE documentation |
| III | Stauss-Grabo et al. 2011 | Acute catarrh of the upper respiratory tract or chronic inflammatory airway disease | 331 | 1 | 11-85 | 10 | Tablets | 5-7.5 : 1 ethanol 30% (m/m) | 75-150 mg | N/A | 2-28 days | Yes | Verbal rating of compliance and tolerability, AE documentation |
| III | Fazio et al. 2009 | Acute and chronic inflammatory bronchial diseases | 10,562 | 905 | 0-98 | 3,287 | Syrup | 5-7.5 : 1 ethanol 30% (m/m) | 52.5 mg (0 - 5 y) 105 mg (6 - 12 y) 105-157.5 mg (> 12 y) | N/A | 7 days | Yes | AE documentation, efficacy and tolerability via questionnaires |
| III | Kraft 2004 | Symptomatic respiratory diseases | 52,478 | N/A | 0-12 | 310 | Syrup | 5-7.5 : 1 ethanol 30% (m/m) | Mean drug dose: 364 mg (1-5 y) 653 mg (6-9 y) 710 mg (> 10 y) | N/A | N/A | N/A | AE documentation |
| III | Büechi/ Kähler 2003 | Acute bronchitis, respiratory diseases accompanied by viscous mucus, cough due to cold | 56 | N/A | 7-93 | 8 | Pastilles | 4-8 : 1 ethanol 30% (m/m) | 52 - 260 mg | N/A | ca. 7 days | Yes | Verbal rating of tussive irritation, sputum amount, consistency and color, efficacy, tolerability, taste |
| III | Hecker et al. 2002 | Chronic bronchitis | 1,350 | 77 | 1-98 | 135 | Effervescent tablets | 5-7.5 : 1 ethanol 30% (m/m) | 97.5 - 130 mg | N/A | 4 weeks | Yes | Verbal rating of development of clinical symptoms, such as cough, sputum, dyspnea and respiratory pain and efficacy and tolerability, AE documentation |
| III | Jahn/Müller 2000 | Infections of upper and/or lower respiratory tract | 372 | 9 | 0-12 | 128 | Syrup | 6-7 :1 N/A | Average values: 25.2 mg (0-1 y) 36 mg (1-4 y) 48.6 mg (4-10 y) 60.3 mg (> 10 y) | N/A | Average: 7.2 days | N/A | Cough and sputum characterization, peak flow profile, verbal rating of tolerability, patient diaries, AE documentation |
| III | Hecker 1999 | Inflammatory or obstructive respiratory disease | 248 | 13 | 0-79 | N/A "multicenter" | Liquid and effervescent tablets | 5-7.5 : 1 ethanol 30% (m/m) | N/A | N/A | Average: 7.3 days (syrup) 8.2 days (effervescent tablets) | N/A | Verbal rating of efficacy and tolerability |
| III | Lässig et al. 1996 | Recidivating obstructive bronchitis | 113 | N/A | 6-15 | 8 | Liquid | 5-7.5 : 1 ethanol 30% (m/m) | 52.5-175 mg | N/A | Up to 30 days | Yes | FVC, $FEV_1$, PEF, $MEF_{25}$, $MEF_{50}$, verbal rating of cough and sputum characteristics, efficacy and tolerability |

* I and II: Controlled clinical studies; III: Uncontrolled clinical studies

BSS is a validated instrument to determine the severity of AB in clinical studies. Investigators score the symptoms of AB in the presence of the patient. It contains patient-reported and investigator-assessed items.[22] VAS is used as a subjective assessment to quantify cough severity. Therefore, patients are asked to mark their impression on a 100-mm scale from "no cough" to "worst cough severity." When evaluating acute cough, the minimal important difference (MID) is defined as 17 mm.[23] Currently, there are limited data to determine the validity of VAS.[24,25] No validity data could be found for VCD.

Results displayed a significantly lower cough severity according to VAS for patients treated with ivy leaf extract compared to the placebo group. This effect was confirmed by BSS and VCD over the treatment period of seven days, and again by VAS over the whole observation period of 14 days. Nevertheless, it is worth noting that cough severity also decreased in the placebo group over the treatment and observation periods. MID for VAS reached 17 mm after three days in the ivy leaf group, and after four days in the placebo group. When analyzing data from each of the five treatment centers separately, no significant difference between the ivy leaf group and placebo group was detected for one center. Treatment compliance was rated "good" because more than 80% of the calculated theoretical intake had been administered to the per-protocol (PP) group. Adverse events (AEs) related to cough, like worsening of cough, middle ear effusion, and sinusitis, were reported for 21 of 181 patients (11.6%; nine in the treament group and 12 in the placebo group).[21]

The efficacy of an add-on treatment with ivy leaf extract in a syrup formulation (Prospan Hustensaft) on lung function in asthmatic children was investigated in another placebo-controlled clinical study.[26] Thirty children (6-12 years of age) who suffered from partial or uncontrolled persistent allergic asthma were enrolled in this randomized, placebo-controlled, double-blind, crossover, monocenter study. The placebo was described as "an inactive, identical flavored, look-alike syrup." One child withdrew from the study during the first treatment period, and five other children showed treatment compliance below 80%. The treatment group received 70 mg of ivy leaf extract daily for 28 to 30 days. The treatment and placebo periods were separated by a washout phase of 28 to 30 days. At the beginning of the run-in phase, all subjects were adjusted to 400 µg of budesonide (a conventional corticosteroid anti-inflammatory drug) daily, which remained the baseline therapy throughout the whole study. Lung function was evaluated by spirometry and body plethysmography before and after bronchodilation. Additionally, patients answered questionnaires about asthma symptoms and quality of life. The Asthma Control Questionnaire (ACQ) reflects some core asthma symptoms and symptom-related clinical markers of asthma.[27] The Pediatric Asthma Quality of Life Questionnaire (PAQLQ) consists of 23 questions that address symptoms, activity limitations, and emotional function.[28,29]

While evaluating treatment effects according to the primary outcome measures (relative change of $FEV_1$ and $MEF_{75-25}$ before bronchodilation), no significant effects of ivy leaf extract were observed. Significant changes were presented in absolute change of $MEF_{75-25}$, $MEF_{25}$, and VC before bronchodilation. The ACQ score decreased significantly in the placebo group, but not in the treatment group. All other evaluated parameters did not differ significantly. The authors conclude that treatment with ivy leaf extract in addition to an inhaled corticosteroid can lead to a significant improvement in lung function parameters in children with mild, persistent, uncontrolled asthma.[26]

Mansfeld et al.[30] conducted a randomized, placebo-controlled, double-blind, crossover, monocenter study to analyze the secretolytic and bronchospasmolytic efficacy and safety of ivy leaf extract in a drop formulation (Prospan Hustentropfen) in 28 asthmatic children (4-12 years of age). Discontinuation of treatment was reported for four patients due to intervening diseases. Patients received a daily dose of 35 mg of ivy leaf extract during a treatment period of three days. A washout phase of three to five days separated the treatment and placebo periods. The main objective was the alteration of lung function determined by respiratory resistance, which was significantly reduced in the treatment group compared to the placebo group at the end of treatment (day three). A significant reduction of intrathoracic gas volume (ITGV) was detected in the treatment group relative to placebo, whereas alterations of residual volume (RV) were not significantly different between groups.

### *Studies with Active Comparators*

In a randomized, double-blind, reference-controlled, multicenter study, Cwientzek et al.[31] compared the efficacy and safety of two marketed ivy leaf extract drop compositions: Hedelix Hustentropfen (Krewel Meuselbach GmbH; Eitorf, Germany; DER 2.2-2.9:1, extraction solvent: ethanol 50% [v/v], propylene glycol [98:2]) and Prospan Hustentropfen. A total of 590 patients (2-86 years of age) across seven sites with AB were recruited and equally distributed to both treatment groups. Overall, 72 drop-outs were reported (35 in the Hedelix group and 37 in the Prospan group). Study medication dosage was determined according to age. The original drop former of the test product Hedelix was exchanged to permit blinding, and, therefore, the number of drops per mL is different from the marketed product. Hence, it is not possible to calculate the exact daily dose for this group. Children in the Prospan group received a daily dose of 25.2 mg (2-4 years of age), 33.6 mg (4-10 years of age), or 50.4 mg (10 years of age or older) of ivy leaf extract over a seven-day treatment period. The authors acted on the assumption that both products contained equivalent drug contents. In contrast to Prospan drops, Hedelix drops contain an ethanol-free fluid extract.

Efficacy was evaluated by investigators via BSS and by patients via VAS rating. Analysis was separately carried out in the intention-to-treat (ITT) and in the PP datasets. No significant differences between the treatment groups or between the ITT and PP datasets could be determined. BSS decreased by approximately 4.7-4.9 points until day seven. Patients rated the efficacy of ivy leaf extract according to VAS from 0 mm (not at all satisfied) to 100 mm (completely satisfied) with a mean of 78.7 ± 22.9 mm for the Hedelix drops group and 76.4 ± 23.7 mm for the Prospan drops group. AEs were reported in 16 of 590 patients (2.7%), with most of these patients suffering from gastrointestinal issues.[31]

**Ivy** *Hedera helix*
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Unkauf and Friedrich[32] conducted a randomized, prospective, multicenter (number of sites not stated) clinical study that evaluated the efficacy and safety of one cough syrup containing ivy leaf extract (Valverde; authorization holder not declared; DER 3-6:1; ethanol 60% [v/v]) against Prospan Hustensaft in 52 children (0-12 years of age) who suffered from dry and painful or productive cough. The exact dose of both medications was not declared. Duration of treatment was 10 days. Outcomes were measured by VAS and a clinical global impression scale (CGI), which addresses disease severity (CGI item I), change of patient status (CGI item II), and ratio of therapeutic effect to AEs (CGI item III). Moreover, cough characteristics, auscultation (listening to respiratory function via stethoscope), AEs, and lab parameters were evaluated. Since 51 of 52 patients showed an improvement in test criteria of at least 50% within 10 days, the authors concluded an equivalent efficacy of both ivy leaf extract preparations.

The efficacy of ivy leaf extract contained in drops and suppositories (Prospan Hustentropfen and Prospan Hustenzäpfchen, respectively) was compared in 26 children (5-11 years of age) with chronic obstructive respiratory diseases in another randomized, crossover, monocenter study by Mansfeld et al.[33] There was no information about dropouts. Patients received a daily dose of 35 mg (drops) or 160 mg (suppositories) of ivy leaf extract over a three-day treatment period. The authors concluded equal efficacy of both formulations in this patient population.

Gulyas et al.[34] analyzed the equivalence of an ivy leaf extract cough syrup and a drop formulation (Prospan Hustensaft and Prospan Hustentropfen, respectively) in a randomized, double-blind, crossover setting. The number of treatment sites was not indicated. Twenty-seven children (10-15 years of age) who suffered from chronic obstructive respiratory disease were included, and the authors reported two dropouts. Children received daily doses of 105 mg of ivy leaf extract in the syrup group and 42 mg in the drops group. Treatment duration was 10 days, and both treatments were separated by a washout phase of two to four days. Lung function parameters ($FEV_1$, FVC, VC, PEF, $R_{AW}$, ITGV, and $sR_{AW}$) were measured, and results displayed a statistically significant difference from the first day to day 10 of treatment for all parameters in both groups. The authors concluded therapeutic equivalence for both groups and since daily doses differed, they hypothesized that the bioavailability of ivy leaf extract is increased by the addition of alcohol.

Meyer-Wegener et al.[35] conducted a double-blind, monocenter clinical study in which the efficacy of ivy leaf extract cough drops (Prospan Hustentropfen) was compared to ambroxol tablets (product not declared) in 99 patients (25-70 years of age) who suffered from chronic bronchitis. One patient was excluded during the study because of prohibited concomitant conventional drug intake. Each group received drops as well as tablets (one of which was a placebo version) in order to maintain the double-blinding nature. Patients received a daily dose of 42-70 mg of ivy leaf extract or took one ambroxol tablet three times daily, with the corresponding placebo formulation, for four weeks. Lung function parameters were measured each week to determine VC, FVC, $FEV_1$ relative to VC, a peak flow profile, and an auscultation report. Additionally, patients kept a diary. The authors concluded equality of both interventions after the treatment period, since they were not able to detect significant differences in lung function parameters between groups. AEs were reported in 13 of 99 patients. The authors did not provide AE details.

Bolbot et al.[36] compared the efficacy and tolerability of ivy leaf extract (Prospan, undeclared formulation) and ACC (product not declared) for the treatment of children with acute obstructive and non-obstructive bronchitis in an open and multicenter study. Fifty children (2-10 years of age) across two sites were included. There was no information about dropouts. Daily doses were 105 mg of ivy leaf extract

or 300-600 mg of ACC (for children 2-6 years of age), or 210 mg of ivy leaf extract or 900-1,200 mg of ACC (for children 7-10 years of age). Treatment started 4.7 days (ivy leaf extract group) or 4.5 days (ACC group) after disease onset and was administered over seven to 10 days. Clinical symptoms, such as cough characteristics, sputum expectoration, shortness of breath, and respiratory pain, were evaluated after seven days and after the full treatment period. In 19 patients in the ivy leaf extract group and 18 patients in the ACC group, external respiration parameters like FVS, $FEV_1$, PEF, $MEF_{25}$, $MEF_{50}$, $MEF_{75}$, and average inhalation weight hour space velocity $(AWSV)_{25-75}$ also were documented after five days and after the full treatment.

Analysis of disease symptoms showed equal values during the treatment period for both groups. After analyzing the external respiration parameters, the authors concluded a superiority of ivy leaf extract compared to ACC concerning its broncholytic activity. The efficacy of ivy leaf extract was rated as "very good" by 40%, "good" by 56%, and "moderate" by 4% of the children. The efficacy of ACC was rated as "very good" by 12.5%, "good" by 66.7%, and "moderate" by 20.8% of the children. The tolerability of ivy leaf extract was rated as "very good" by 40% and "good" by 60% of the investigators, and the tolerability of ACC was rated as "very good" by 12%, "good" by 64%, "moderate" by 20%, and "poor" by 4% of the investigators.[36]

Maidannik et al.[37] conducted an open, multicenter (two sites) clinical study that addressed the efficacy of an ivy leaf extract cough syrup preparation (Prospan Hustensaft) in relation to ambroxol syrup (product not declared) in children (0-15 years of age) with acute or chronic respiratory disease. In parallel, 30 of the 72 enrolled children suffered from concomitant diseases and partially received antibiotics. There was no information about dropouts. Ivy cough syrup was given to 53 children and ambroxol to 19. The daily dose of ambroxol syrup was not declared, and no precise amount of ivy leaf extract could be derived from the declaration that three teaspoons (for children 1-6 years of age) or six teaspoons (for children 7-14 years of age) of the cough syrup were administered daily. The treatment period was seven to 10 days for acute and 10-14 days for chronic conditions, and medication started three to four days after the onset of illness.

Patient condition was documented once a day, and an evaluation of clinical efficacy according to a four-point scale (excellent, good, poor, no effect) was conducted on days three, seven, and 14. For the Prospan group, no effect was reported in 3.3% of patients and, depending on the assessor, efficacy was rated as 90.1% by physicians and 87.1% by patients or their parents. Additionally, a normalization of leukocyte count after 7 ± 1.5 days for all patients was observed. The authors concluded that the ivy leaf extract preparation had broncholytic activity because the external respiration weight space velocity normalized during the treatment of patients with obstructive abnormalities. No significant difference between treatments was observed in terms of decreasing symptoms of productive cough. More than 50% of patients were cough-free after seven days, and all were cough-free after 14 days in both treatments groups.[37]

***Observational Studies***

Schmidt et al.[38] conducted two independent open, non-interventional, multicenter (14 sites) clinical studies that analyzed the tolerability and safety of two different formulations of an ivy leaf extract (Hedelix syrup and drops) in children (0-13 years of age) who suffered from acute respiratory catarrh and/or chronic recurrent inflammatory bronchial disease. The syrup formulation was given to 133 children, and the drops were given to 135 children. Fifteen patients were excluded from the study. Children received a daily extract dose of 50 mg (0-1 year of age), 150 mg (1-4 years of age), 200 mg (4-10 years of age), or 300 mg (10-13 years of age) for an average treatment period of 10 days. Tolerability and safety were evaluated via a verbal rating scale by each patient, their caregivers, and physicians. Five AEs were recorded during these studies; four of these were gastrointestinal issues, and one patient suffered from angular cheilitis (lip inflammation) and diaper dermatitis. In 98.2% or 99.2% of patients receiving syrup and 96.9% or 100% of patients receiving drops, a good to very good tolerance was reported at the final visit depending on the respondent, either patient or physician.

Stauss-Grabo et al.[39] conducted an observational, multicenter (10 sites) study that evaluated the tolerability of film-coated tablets (Prospan) that contained 25 mg of ivy leaf extract each for the treatment of catarrh of the upper respiratory tract accompanied by cough, chronic bronchitis, COPD, pneumonia, or AB. A total of 331 patients (11-85 years of age) were included, and one dropout was reported. The treatment dose varied. A total of 310 patients received at least seven days of treatment: 113 patients with a twice-daily dose of two tablets, 196 patients with a dose of two tablets three times per day, and one patient with a dose of one tablet three times per day. The overall treatment duration was two to 28 days, with 126 patients receiving two tablets twice per day, 203 patients with a dose of two tablets three times daily, and one patient with one tablet three times per day. The median treatment duration was eight days. Concomitant diseases were reported for 20 patients. No serious AEs were reported, but one patient suffered from nausea during treatment. Tolerability was rated as "very good" or "good" by 95.4% of patients and 98.5% of physicians. Patient compliance was rated as "good" by 99.1% of the physicians and "moderate" by 0.9% of the physicians. The authors concluded that the ivy leaf extract that was investigated is safe and very well tolerated in the studied population.

Fazio et al.[40] demonstrated the tolerability and safety of an ivy cough syrup formulation (Prospan Hustensaft) in an open, multicenter (3,287 sites) post-marketing study with 10,562 included patients (0-98 years of age) recruited by physicians in 11 Latin American countries. Because they did not participate in follow-up visits, 905 patients were not evaluated. Among the patients were 5,181 children (0-14 years of age) with acute or chronic bronchial inflammatory disease associated with hypersecretion of mucus and productive cough (which is frequently associated with an infectious agent), and

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patients with cough alone. The daily doses of ivy leaf extract were 52.5 mg (for children 0-5 years of age), 105 mg (6-12 years of age), and 105-157.5 mg (older than 12 years of age) for a seven-day treatment period. Concomitant conventional drug intake was reported for 5,865 patients, whereas 3,795 patients received antibiotics. AEs were reported in 2.1% of all patients and in 1.2% of children. These AEs were mainly gastrointestinal issues and allergic skin symptoms. Additionally, these patients reported dry mouth and thirst, anorexia, eructation (belching), stomatitis, anxiety, headache, drowsiness, palpitation, sweating, and other AEs. The majority (96.6%) of the study population tolerated the therapy well. The occurrence of AEs increased when conventional drugs, especially antibiotics, were used.

A retrospective, multicenter (310 sites) data acquisition presented by Kraft[41] evaluated the tolerability of an ivy leaf extract cough syrup (Prospan Hustensaft) in 52,478 children (0-12 years of age) with symptomatic respiratory diseases. The mean drug dose was 364 mg (1-5 years of age), 653 mg (6-9 years of age), and 710 mg (10 years of age or older). Among this population, 115 AEs were reported, with about 77% suffering from gastrointestinal issues and about 18% exhibiting allergic skin rashes (exanthema and urticaria).

Several other post-marketing surveillance studies that focused on the treatment of different respiratory diseases with diverse formulations of ivy leaf extracts present an overall "good" to "very good" tolerability stated by investigators and patients.[42-45] AEs reported in these studies were gastrointestinal issues and allergic exanthema.[43-45] Besides allergic exanthema and urticaria, other allergic side effects of ivy leaf formulations, such as dyspnea, have also been reported.[14] Some studies reported low numbers of dropouts due to a lack of therapeutic efficacy.[40,44,46]

## Discussion

Clinical research on the efficacy and safety of ivy leaf preparations for the therapy of respiratory diseases dates back to the 1950s.[18,19] The clinical studies reviewed here were published between 1993 and 2016. Since the underlying study designs vary, we separated all reviewed studies into two major groups: controlled and non-controlled studies. An adequate study design that includes an appropriate control is a prerequisite to determine the efficacy of a treatment, and, therefore, controlled studies were evaluated according to their relevance for safety and efficacy, whereas non-controlled studies were reviewed to assess only information on treatment safety. Besides the absence of a control, observational and non-interventional studies of marketed herbal medicinal products that contain ivy leaf extract are open data collections in practice; this study design is not capable of providing a strong basis to evaluate the overall efficacy. Since acute respiratory diseases are mostly of a self-limiting nature, the difficulty of finding an adequate study design must be acknowledged when evaluating data reliability. In the context of this self-limiting nature, clinical investigations can only prove a more rapid healing in contrast to controls.

## Clinical Efficacy

### *Acute Respiratory Disease (Acute Cough)*

Just two of the 19 reviewed studies were carried out in a randomized controlled design; one was placebo-controlled[21] and the other was reference-controlled.[31] Both determined cough severity via BSS and, based on the results obtained, the authors were able to conclude an improvement in the treatment groups within seven days of treatment.

Schaefer et al.[21] demonstrated a BSS improvement of 8.4 in the treatment group, compared to 5.8 in the placebo group after seven days of treatment, but in this study a 20% improvement according to BSS in the treatment group was also shown in relation to a 10% improvement in the placebo group after 48 hours. Although the results of this study present the only data on efficacy in acute cough with a certain level of evidence, it also suffers from design flaws, like the questionable blinding and application of statistical methods. BSS seems to be the only validated score used in the Schaefer et al. study (scores like VAS, VCD, and GEA are not considered validated assessment tools).

Since Cwientzek et al.[31] did not present absolute data, it is difficult to assess efficacy, especially according to the known BSS improvement for the placebo group from the Schaefer et al.[21] study. Moreover, it is difficult to determine comparability of drug doses for the products in this study, because a calculation of the exact drug dose for the Hedelix group is not possible, since the original drop former was exchanged for the test product to permit blinding. Even though both studies included more patients than most other studies, statistically verified patient numbers would be desirable.

The definition of an adequate reference control for the determination of efficacy is a stumbling block. Bolbot et al. concluded that the ivy leaf extract (Prospan) and ACC had equal mucolytic activity.[36] The mucolytic efficacy of ACC and other mucolytic agents has been reported, but the clinical benefits are a matter of scientific debate.[47] Therefore, reporting an equal effect of ivy leaf extracts and standard mucolytics is not sufficient without simultaneously presenting superiority against placebo in the same setting. Moreover, the treatment started 4.5 to 4.7 days after disease onset in this study, which is late in the context of this self-limiting disease. Bolbot et al. also reported that ivy leaf extract (Prospan) had superior spasmolytic activity, as determined by spirometric analysis. Although this effect is reasonable, performing spirometric assessments with young children is challenging. Moreover, patient selection criteria for spirometric analysis are non-transparent and therefore permit selection bias.

### *Chronic Respiratory Disease*

Among the 19 reviewed clinical studies, six focused on chronic respiratory diseases, five of which were conducted in a randomized and controlled study design. Two of the six studies evaluated the efficacy of ivy leaf extract in children who suffered from chronic obstructive respiratory disease.[33,34] Both studies were randomized, controlled, crossover studies that compared the efficacy of two ivy leaf extract (Prospan) formulations, and both had severe

study design flaws according to current clinical trial design standards. Definitions of chronic respiratory diseases have changed over the years, and different opinions about their classification still exist.[8,48] According to the current definition of COPD, for example, the disease rarely affects children.[12] No effective conclusion about the efficacy of ivy leaf extract in patients suffering from COPD can be drawn from the evaluation of the endpoints presented in these studies, since inclusion criteria did not match the current definition of COPD. Daily dose and/or route of administration of the diverse ivy leaf extract formulations (e.g., syrup, drops, tablets, or suppositories) compared here clearly differ. It would have been necessary to either administer the same doses or prove an equal "bioavailability" of unequal doses due to different routes of administration. (In this context, the term "bioavailability" is not accurate when talking about an extract formulation that contains a multitude of ingredients.) Moreover, the washout phase was relatively short (two to four days) in both studies, so carryover effects may have played a role. To evaluate efficacy from these data is challenging due to missing placebo control, low patient numbers, and concomitant conventional drug intake.

Another randomized, double-blind, monocenter, ambroxol-controlled study evaluated the efficacy of an ivy leaf extract (Prospan) for the treatment of chronic bronchitis.[35] The authors concluded equivalence for both treatments since they were not able to detect significant differences in spirometric, auscultation, or diary analyses. Unfortunately, this publication did not present any details about the exact dose of the active comparator ambroxol. The challenge with standard mucolytic reference controls was described previously. Consequently, a beneficial bronchospasmolytic effect for the therapy of chronic obstructive bronchitis was not observed with either of the two preparations.

In two studies, the efficacy of an ivy leaf extract (Prospan) in asthmatic children was assessed.[26,30] Both were randomized, placebo-controlled, double-blind, crossover studies in which body plethysmography and spirometry were used to determine improvements in lung function. Mansfeld et al.[30] found a statistically significant reduction of $R_{AW}$ and ITGV after three days of therapy with ivy leaf extract. Spirometric parameters did not differ significantly. The PP analysis included only 24 patients. The authors presented insufficient information about statistical methods. A treatment period of three days in a chronic, paroxysmal obstructive disease is short, and a single visit is not sufficient to assess treatment efficacy since asthma is characterized as an alternating daily condition. Moreover, a washout phase of three to five days may result in confounding carryover and treatment effects.

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Zeil et al.[26] included 30 asthmatic children (6-12 years of age), although six protocol violations were reported (20% of the overall study population). Baseline therapy was budesonide, and ivy leaf extract (Prospan) was examined as an add-on therapy to enhance lung function. Partially improved lung function after four weeks of treatment was determined. Data were obtained according to the ITT analysis, without declaring the procedure for dropout values. Moreover, a drawback of ACQ is the rating period since patients evaluate symptoms from the previous seven days; a shorter period or daily rating would be more desirable to evaluate variable asthma symptoms.[27] Because of the non-crossover analysis and the small study population, the data presented are not convincing to determine the efficacy of ivy leaf extract as an add-on therapy for asthmatic children. This study concept implicates a risk that budesonide baseline therapy might mask potential advantageous effects of the add-on therapy with ivy leaf extract. This, however, has no bearing on the positive outcome of the study. The changes in absolute lung function parameters may be promising enough to conduct more studies with a larger patient population and more stringent study design to determine a benefit for asthmatic children.

### *Non-Homogeneous Patient Population (Acute and Chronic Respiratory Disease)*

As previously mentioned, the evaluation of treatment effects is especially difficult when diverse patient populations are pooled and analyzed together. In two studies, investigators tried to assess the efficacy of ivy leaf extracts (Prospan and Valverde) for the therapy of acute or chronic respiratory diseases,[37] or dry and painful or productive cough,[32] with small study populations in an open setting. Both studies fail to provide diagnostic details and the exact daily doses of all medications. The authors at least partially justified the efficacy of the therapy with a treatment success of about 50% of patients after seven days.[32] This argument is especially controversial when talking about a disease that is self-limiting to some extent. Concomitant diseases and drug intake also were reported in various cases,[37] or this information was not presented at all.[32] Parameter evaluation was based mainly on invalid scores or verbal ratings. Maidannik et al.[37] presented a non-homogenous allocation to treatment groups and treatment duration. Treatment started three to four days after disease onset, which seems to be late and is also confusing, taking the patients with chronic conditions into account.[37] Altogether, a conclusion based on evidence-based criteria about any treatment efficacy is difficult with these severe flaws in study design according to current clinical trial standards.

## Summary

Most of the controlled clinical studies discussed here in terms of efficacy investigated a similar ivy leaf extract, Prospan, marketed in different formulations. Further details on extract manufacture are not available, and no statements were provided regarding the similarity of extracts used in the products administered apart from extract solvent (ethanol 30% [w/w]) and DER (5-7.5:1). This extract is also listed as extract "a" in the EU HMPC monograph.

A certain degree of efficacy of ivy leaf extract was demonstrated in only one study: a randomized, placebo-controlled, double-blind and multicenter study in adults with acute cough based on a validated score to evaluate AB severity.[21] The outcome of the study clearly indicates an efficacy of ivy leaf extract in reducing cough severity and, therefore, a benefit in the treatment of acute cough. An additional recording of lung function parameters would have been desirable to corroborate these effects.

Data obtained from all other reviewed studies that focused on AB or obstructive diseases like asthma or COPD were not convincing and did not conclusively establish therapeutic effects in an evidence-based manner. Drawbacks of these studies include non-homogenous patient populations according to diagnosis and/or age,[28-31,33-35] concomitant diseases or drug intake,[26,36] and lack of appropriate controls. Presenting equivalence of ivy leaf extract and other expectorants that contain ambroxol or ACC is not meaningful when superiority over placebo is not established in the same study design.

Assessing cough severity is challenging. Validated scores are essential to obtain reliable results. BSS is a validated method to assess AB severity.[22] Other scores used are not valid and, therefore, less useful in support of clinical effects.

One study was designed to compare different formulations (suppositories versus drops) of ivy leaf extracts without

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discussing the possible impact of these different routes of administration in terms of systemic availability of putative active constituents in the extract.[33]

The relevance of data supplied by many studies suffers from low numbers of patients or investigation sites.[26,30,32,33,36] Results presented in these studies can serve only as a lead; more robust evidence might be established in clinical trials with larger patient populations. Another drawback is the open study design.[33,36] In most studies, no indication regarding blinding of placebo and active treatment was given.

## Clinical Safety

### *Tolerability*

The tolerability of ivy leaf extracts (Prospan and Hedelix) in formulations tested was overall rated "good" to "very good" in the vast majority of cases.[31,33,36,38-40] Discontinuation of treatment was reported for four patients due to intercurrent diseases.[30]

### *Adverse Events*

None of the reported AEs were classified as serious. AEs occurred in one of 330,[39] five of 272,[38] 16 of 590,[31] and 115 of 52,478[41] patients. Most of the AEs reported were gastrointestinal side effects, but allergic reactions were also described. In one study, worsening of cough, middle ear effusion, and sinusitis were reported in 21 of 181 patients.[21] Meyer-Wegener et al. reported AEs in 13 of 99 patients, but did not disclose any details.[35]

Two observational studies are of special interest, because a large number of patients was evaluated and relatively high daily doses of ivy leaf extract (Prospan) were administered.[40,41] The HMPC herbal monograph recommends a daily extract dose of 24-36 mg (2-5 years of age), 33-70 mg (6-11 years of age), or 45-105 mg (12 years of age or older).[14] Fazio et al. described daily extract doses of 52.5 mg (0-5 years of age), 105 mg (6-12 years of age), or 105-157.5 mg (12 years of age or older),[40] and Kraft described mean daily drug doses of 364 mg (1-5 years of age), 653 mg (6-9 years of age), or 710 mg (10 years of age or older).[41] AEs were reported in 203 of 9,657[40] and 115 of 52,478 patients,[41] respectively. These AEs were also mainly gastrointestinal disorders and allergic skin symptoms. Besides these, Fazio et al.[40] reported AEs such as dry mouth and thirst, anorexia, eructation, stomatitis, anxiety, headache, drowsiness, palpitation, sweating, and others. AEs led to discontinuation of therapy in 46 cases and were increased when additional drugs, especially antibiotics, were prescribed. Overall, 388 patients discontinued treatment, mostly because of improvement (186 patients), lack of efficacy (76 patients), or worsening (39 patients). One drawback of this study is the high dropout rate (905 patients). This might have an effect on the number of AEs reported. Furthermore, the patient population was non-homogenous in terms of age and symptoms, and concomitant drug intake was recorded in 60.7% of patients.[40]

### *Contraindications and Precautions*

To limit the risk of AEs, some precautions should be considered. According to European regulations, children younger than two years of age should not receive secretolytic agents because of the risk of aggravation of respiratory symptoms. Medical diagnosis is necessary before therapy in cases of recurrent or persistent cough in young children (2-4 years of age) and if dyspnea, fever, or purulent sputum occur. If hypersensitivity to substances originating from the Araliaceae family is known, alternative treatments should be used. The concomitant use of opioids or active ingredients derived from opioids, like codeine or dextromethorphan, is not recommended without medical advice. Due to the prevalence of gastrointestinal side effects, patients with gastritis or gastric ulcers should be treated with care. Since there are no sufficient safety data, ivy leaf extracts should not be used during pregnancy or lactation. Children under six years of age should not receive liquid ivy leaf extract preparations with a DER of 1:1 and ethanol 70% (v/v) as the extraction solvent because of the alcohol content. Overdose may induce nausea, vomiting, diarrhea, and/or agitation.[14]

Aggression and diarrhea after an accidental intake of an ivy leaf extract (reported DER 4-8:1; extraction solvent: ethanol 30% (m/m)) corresponding to 1.8 g of herbal substance was reported for one four-year-old child.[15]

## Conclusion

Ivy leaf extracts have shown effects in vitro that may correspond to secretolytic and bronchospasmolytic clinical effects. Many clinical studies have been carried out to confirm these effects. Unfortunately, most of these studies lacked an appropriate design to support the proposed effects in an evidence-based manner. Regardless of their evidence level, most of the reviewed clinical studies determining the efficacy and/or safety of ivy leaf extracts for the therapy of respiratory diseases accompanied by cough are of low quality due to significant design flaws according to current standards.

However, one of the 19 reviewed studies was performed in a randomized, placebo-controlled, multicenter, and double-blind design. The study was conducted with Prospan Hustenliquid. Based on the results obtained, the authors were able to convincingly demonstrate an effective reduction of cough severity in adults who suffered from acute cough, although some of the applied scores are of debatable validity to evaluate bronchitis severity. While results should be confirmed in further studies with appropriate design, these data strongly suggest a secretolytic effect in acute cough.

The efficacy of ivy leaf extracts in chronic respiratory diseases is still unclear, and we could not find more than a promising lead while reviewing clinical data. No serious AEs were described. Since AEs were rare and not serious, mostly related to gastrointestinal disorders or allergic reactions, we conclude that the short-term (up to seven days) application of the investigated ivy leaf extracts discussed in this article presents a negligible risk in the treatment of acute respiratory diseases accompanied by cough. Further research should include the objective of exacerbation prophylaxis to gain more helpful information about potential benefits for patients who suffer from chronic respiratory diseases. HG

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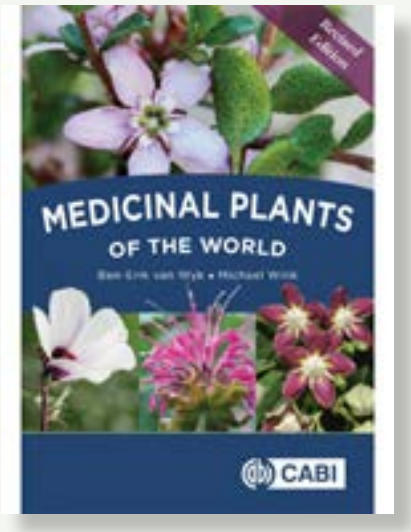
## References

1. Wichtl M. *Hederae folium. Ivy leaf.* In: *Herbal Drugs and Phytopharmaceuticals.* 3rd ed. Stuttgart: Medpharm GmbH; 2004:274-277.
2. Sticher. Efeublätter. *Hänsel/Sticher Pharmakognosie, Phytopharmazie*. Wissenschaftliche Verlagsgesellschaft Stuttgart; 2015.
3. Wichtl M. *Hederae folium. Wichtl – Teedrogen und Phytopharmaka.* Wissenschaftliche Verlagsgesellschaft Stuttgart; 2016.
4. Schulte-Michels J, Wolf A, Aatz S, et al. Alpha-hederin inhibits G protein-coupled receptor kinase 2-mediated phosphorylation of beta2-adrenergic receptors. *Phytomed.* 2016;23(1):52-57.
5. Sieben A, Prenner L, Sorkalla T, et al. Alpha-hederin, but not hederacoside C and hederagenin from *Hedera helix*, affects the binding behavior, dynamics, and regulation of beta 2-adrenergic receptors. *Biochemistry.* 2009;48(15):3477-3482.
6. Wolf A, Gosens R, Meurs H, Haberlein H. Pre-treatment with alpha-hederin increases beta-adrenoceptor mediated relaxation of airway smooth muscle. *Phytomed.* 2011;18(2-3):214-218.
7. Greunke C, Hage-Hulsmann A, Sorkalla T, Keksel N, Haberlein F, Haberlein H. A systematic study on the influence of the main ingredients of an ivy leaves dry extract on the beta2-adrenergic responsiveness of human airway smooth muscle cells. *Pulmonary Pharmacology & Therapeutics.* 2015;31:92-98.
8. Deutsche Gesellschaft für Allgemeinmedizin und Familienmedizin. Husten - DEGAM-Leitlinie Nr. 11. Düsseldorf Omicron publishing 2014:1-80.
9. Kardos P, Berck H, Fuchs KH, et al. Guidelines of the German Respiratory Society for diagnosis and treatment of adults suffering from acute or chronic cough. *Pneumologie.* 2010;64(11):701-711.
10. Miller MR, Hankinson J, Brusasco V, et al. Standardisation of spirometry. *The European Respiratory Journal.* 2005;26(2):319-338.
11. Criee CP, Sorichter S, Smith HJ, et al. Body plethysmography—its principles and clinical use. *Respir Med.* 2011;105(7):959-971.
12. Vogelmeier C. Leitlinie der Deutschen Atemwegsliga und der Deutschen Gesellschaft für Pneumologie und Beatmungsmedizin zur Diagnostik und Therapie von Patienten mit chronisch obstruktiver Bronchitis und Lungenemphysem (COPD). In: Deutsche Atemwegsliga; Deutsche Gesellschaft für Pneumologie und Beatmungsmedizin, 2007.
13. Buhl R. Leitlinie zur Diagnostik und Therapie von Patienten mit Asthma. In: *Deutsche Atemwegsliga*. Deutsche Gesellschaft für Pneumologie und Beatmungsmedizin, 2006.
14. HMPC. European Union herbal monograph on *Hedera helix* L., folium EMA/HMPC/586888/2014.
15. HMPC. Final Assessment Report on *Hedera helix* L. Folium. EMA/HMPC/586887/2014.
16. Gulyas A. Efeublätter-Extrakt zeigt bei Kindernmit chronisch obstruktiven Atemwegserkrankungen vergleichbare Effekte wie Acetylcystein. 1999.
17. Roth R. Efeublätter wirken sekretolytisch und bronchospasmolytisch - Anwendungsbeobachtung bestätigt Wirksamkeit der Behandlung mit Efeublätter-Trockenextrakt. *Pädiatrische Nachrichten.* 2000;Sonderdruck:1-3.
18. Rath F. Klinische Prüfung der Wirksamkeit des Hustenmittels Prospan. *Fortschritte der Therapie.* 1968;22:1015-1016.
19. Stöcklin P. Klinische Erfahrungen mit dem Hustenmittel Prospan. *Praxis.* 1959;41:934-938.
20. Network SIG. Critical appraisal: Notes and checklists. 2014; www.sign.ac.uk/methodology/checklists.html. Accessed 16.11.16, 2016.
21. Schaefer A, Kehr MS, Giannetti BM, Bulitta M, Staiger C. A randomized, controlled, double-blind, multi-center trial to evaluate the efficacy and safety of a liquid containing ivy leaves dry extract (EA 575®) vs. placebo in the treatment of adults with acute cough. *Die Pharmazie - An International Journal of Pharmaceutical Sciences.* 2016;71(9):pp. 504-509(506).
22. Lehrl S, Matthys H, Kamin W, Kardos P. Assessment of the effect of pharmacotherapy in common cold/acute bronchitis - the Bronchitis Severity Scale (BSS). *Pneumologie.* 2014;68(8):542-546.
23. Spinou A, Birring SS. An update on measurement and monitoring of cough: what are the important study endpoints? *J Thorac Dis.* 2014;6(Suppl 7):S728-734.
24. Leconte S, Ferrant D, Dory V, Degryse J. Validated methods of cough assessment: a systematic review of the literature. *Respiration.* 2011;81(2):161-174.

25. Schmit KM, Coeytaux RR, Goode AP, et al. Evaluating cough assessment tools: a systematic review. *Chest.* 2013;144(6):1819-1826.
26. Zeil S, Schwanebeck U, Vogelberg C. Tolerance and effect of an add-on treatment with a cough medicine containing ivy leaves dry extract on lung function in children with bronchial asthma. *Phytomed.* 2014;21(10):1216-1220.
27. Globe G, Martin M, Schatz M, et al. Symptoms and markers of symptom severity in asthma--content validity of the asthma symptom diary. *Health Qual Life Outcomes.* 2015;13:21.
28. Juniper EF, Guyatt GH, Feeny DH, Ferrie PJ, Griffith LE, Townsend M. Measuring quality of life in children with asthma. *Qual Life Res.* 1996;5(1):35-46.
29. La Scala C, Naspitz C, Solé D. Adaptation and validation of the Pediatric Asthma Quality of Life Questionnaire (PAQLQ) in Brazilian asthmatic children and adolescents. *J Pediatr (Rio J)* 2005;81:54-60.
30. Mansfeld HJ, Höhre H, Repges R, Dethlefsen U. Therapie des Asthma bronchiale mit Efeublätter-Trockenextrakt. *Münchener Medizinische Wochenzeitschrift.* 1998;140(3):26-30.
31. Cwientzek U, Ottillinger B, Arenberger P. Acute bronchitis therapy with ivy leaves extracts in a two-arm study. A double-blind, randomised study vs. an other ivy leaves extract. *Phytomed.* 2011;18(13):1105-1109.
32. Unkauf M, Friedrich M. Bronchitis in children—clinical study of dry extract of ivy. *Der Bayerische Internist.* 2000;4:2-4.
33. Mansfeld HJ, Höhre H, Repges R, Dethlefsen U. Sekretolyse und Bronchospasmolyse. *Therapiewoche Pädiatrie.* 1997;10(3):153-157.
34. Gulyas A, Repges R, Dethlefsen U. Konsequente Therapie chronisch-obstruktiver Atemwegserkrankungen bei Kindern. *Atemwegs- und Lungenkrankheiten.* 1997;23(5):291-294.
35. Meyer-Wegener J. Efeu versus Ambroxol bei chronischer Bronchitis. *Zeitschrift für Allgemeinmedizin.* 1993;69(3):61-66.
36. Bolbot Y, Prokhorov E, Mokia S, Yurtseva A. Comparing the efficacy and safety of high-concentrate (5-7.5:1) ivy leaves extract and Acetylcysteine for treatment of children with acute bronchitis. *Drugs of Ukraine.* 2004;11:1-4.
37. Maidannik V, Duka E, Kachalova O, Efanova A, Svoykina S, Sosnovskaja T. Efficacy of Prospan application in children's diseases of respiratory tract. *Pediatrics, Toxicology and Gynecology.* 2003;1-7:1-7.
38. Schmidt M, Thomsen M, Schmidt U. Suitability of ivy extract for the treatment of paediatric cough. *Phytotherapy Research: PTR.* 2012;26(12):1942-1947.
39. Stauss-Grabo M, Atiye S, Warnke A, Wedemeyer RS, Donath F, Blume HH. Observational study on the tolerability and safety of film-coated tablets containing ivy extract (Prospan Cough Tablets) in the treatment of colds accompanied by coughing. *Phytomed.* 2011;18(6):433-436.
40. Fazio S, Pouso J, Dolinsky D, et al. Tolerance, safety and efficacy of Hedera helix extract in inflammatory bronchial diseases under clinical practice conditions: a prospective, open, multicentre postmarketing study in 9657 patients. *Phytomed.* 2009;16(1):17-24.
41. Kraft K. Verträglichkeit von pflanzlichen Drogen für akute Erkrankungen der Atemwege im Kindesalter. *Zeitschrift für Phytotherapie.* 2004;25:179-181.
42. Buechi S, Kahler D. Efeu (*Hedera helix*) bei Atemwegserkrankungen. *Schweizerische Zeitschrift für Ganzheitsmedizin.* 2003;15(3):124-128.
43. Hecker M. Wirksamkeit und Verträglichkeit von Efeuextrakt bei Patienten mit Atemwegserkrankungen. *Natura Med.* 1999;14(2):28-33.
44. Hecker M, Runkel F, Völp A. Behandlung chronischer Bronchitis mit einem Spezialextrakt aus Efeublättern - multizentrische Anwendungsbeobachtung mit 1350 Patienten. *Forschende Komplementärmedizin und Klassische Naturheilkunde.* 2002(9):77-84.
45. Jahn E, Müller B. Efeublättertrockenextrakt. *Deutsche Apotheker Zeitung.* 2000;140(12):135-138.
46. Lässig W, Generlich H, Heydolph F, Paditz E. Wirksamkeit und Verträglichkeit efeuhaltiger Hustenmittel - Prospan Kindersaft bei rezidivierenden obstruktiven Atemwegserkrankungen. *Therapiewoche Pädiatrie.* 1996;9:489-491.
47. Rogers DF. Mucoactive agents for airway mucus hypersecretory diseases. *Respiratory Care.* 2007;52(9):1176-1193; discussion 1193-1177.
48. WHO. GOLD Guideline. Global Initiative for Chronic Obstructive Lung Disease. 2006.

***Medicinal Plants of the World: An Illustrated Scientific Guide to Important Medicinal Plants and Their Uses*, 2nd edition**, by Ben-Erik van Wyk and Michael Wink. Wallingford, UK: CABI; 2017. Hardcover, 520 pages. ISBN: 9781786393258. $50.00.




This is a revision of the 2004 text, which was reviewed in *HerbalGram* issue 62.[1] Both authors are medicinal plant experts. Ben-Erik van Wyk, PhD, is a professor of botany at the University of Johannesburg in South Africa. He is a prolific author of books on the ethnobotany of southern Africa and other titles on plants of Africa and other areas of the world. Michael Wink, PhD, is director of the Institute of Pharmacy and Molecular Biotechnology at Heidelberg University in Germany.

Depending on the reader's interpretation, the title appears to be a bit ambitious, possibly suggesting that this book might contain all or most of the medicinal plants of the world. Such an undertaking, however, is well beyond the actual scope of this book and its previous version. *Medicinal Plants of the World* contains entries on more than 350 medicinal plants (28 more than were covered in the first edition) of all regions of the earth, hence a more rational and limited interpretation of the title.

This edition is profuse with color photographs and boasts more than 230 new photos that were added to the more than 500 in the previous edition. Each plant is given a one-page profile that includes: Latin name, family name, European common names, plant description, origin, part(s) used, therapeutic category, uses and properties, preparation and dosage, active ingredients, pharmacological effects, warnings (when applicable), notes, and status in traditional and/or modern medicine.

For a volume that attempts to take a global perspective on medicinal plants, the regulatory section tends to be a bit Eurocentric, with references to monographs of the German Commission E, European Scientific Cooperative on Phytotherapy (ESCOP), and European Committee on Herbal Medicinal Products (HMPC), as well as to the 8th edition of the *European Pharmacopoeia* (PhEur8). However, this may be understood with the awareness that the European compendia tend to provide the most up-to-date and reliable information on medicinal plants. The monographs of the World Health Organization (WHO) and references to international pharmacopeias add information on medicinal herbal preparations in non-European areas.

Additional sections discuss medicine systems of the world, plant parts, dosage forms, use of medicinal plant products, active ingredients, quality control and safety, efficacy of medicinal plants, regulation of herbal remedies and phytomedicines, health disorders and medicinal plants, and secondary metabolites and their effects. The book also includes an extensive "quick guide" to commercialized medicinal plants, a glossary, a bibliography, and an extensive index.

Designed as a "quick reference guide," this book provides a plethora of relevant data on a representative subset of the world's medicinal plants, supported by citations that lead the reader to more detailed information and photos that show the plants' morphology. Thus, I highly recommend this text as a starting point for further investigation. HG

**—Mark Blumenthal**
**ABC Founder and Executive Director**
**Austin, Texas**

## Reference

1. González-Stuart A. *Medicinal Plants of the World* by Ben-Erik Van Wyk and Michael Wink. *HerbalGram*. 2004;62:73. Available at: http://cms.herbalgram.org/herbalgram/issue62/article2691.html. Accessed January 8, 2018.

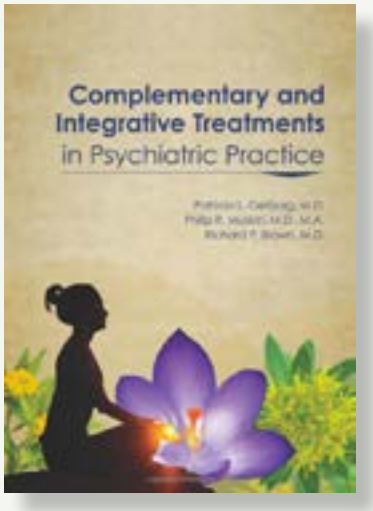
***Complementary and Integrative Treatments in Psychiatric Practice*** by Patricia Gerbarg, Philip Muskin, and Richard Brown, eds. Washington, DC: American Psychiatric Association Publishing; 2017. Softcover, 425 pages. ISBN: 978-1-61537-031-3. $65.00.

As more psychiatrists feel limited by the modern psychopharmacological model that predominates current practice, interest in the field of integrative psychiatry has grown significantly. Psychiatry, as a profession, had been slow to begin the transformation to integrative medicine and a more holistic approach. This process is a paradigm shift that moves practitioners from a disease-oriented model to a health-oriented model. For example, five years ago, I reviewed existing conventional psychiatric textbooks and found no discussion of nutrition, micronutrients, or herbal medicine. This textbook, published by the American Psychiatric Association's publishing arm, supports a practice in which natural modalities such as herbal medicine are acknowledged and more available.

In this text, the editors, all deeply experienced and accomplished, have selected a wide range of professionals to author the 29 chapters. The topics range from specific and quite narrow (*Sceletium tortuosum* [Aizoaceae] and *Bacopa monnieri* [Plantaginaceae] for cognitive support) to quite broad ("Complementary and Integrative Medicine in Child and Adolescent Psychiatric Disorders"). The cover-

age is effectively executed with deep and thorough references included at the end of each chapter.

Herbal medicine is well-represented here. Mark Blumenthal provides introductory comments about plant medicines, and he explores topics such as regulation, research quality, adulterants, analytical testing, and phytoequivalence (the equivalence of a plant-based medicine to a conventional medicine), as they relate to a mental health-oriented practice. Seven chapters go into depth on various herbal remedies. Herbalists may find that the traditional history and application of these plant medicines are replaced with the biochemistry and bench science more comfortable to those in academia.




Many of the authors are researchers who are familiar with the latest science, but less comfortable in the hazy realm of clinical application to practice. In my experience, edited medical textbooks like this tend to fall to one side of the "town/gown" divide; that is, they tend to favor either researchers or clinicians. It is very difficult to serve both sides of that divide well. Some of the chapters in this book found that balance. For example, "Single and Broad-Spectrum Micronutrient Treatments in Psychiatric Practice" by Charles Popper, MD, Bonnie J. Kaplan, PhD, and Julia J. Rucklidge, PhD, presents the existing research quite well and then delves into the actual clinical uses of these tools in solid detail, with step-by-step guidance for application. They even include a discussion of obtaining informed consent. Overall, the text functions best as an introduction and reference for the relevant research on these clinical tools, rather than how they are best applied in practice.

This book may be the ideal gift for a psychiatrist friend who is just beginning to explore these realms, since it offers a worthy introduction to these topics. Well-designed to be widely accepted by practitioners who are unfamiliar with integrative topics, it leads with references and hard science.

Some of the more cutting-edge topics in integrative mental health are not addressed: the microbiome and gut health as they relate to psychiatric symptoms; systemic inflammation and its relationship to chronic psychiatric illness; and psychoactive medicines, such as psilocybin mushrooms, and the research linking them to significant mental health benefits for anxiety, depression, and end-of-life issues. These topics have less direct pathways to clinical application, but the evolving science cannot be denied.

All in all, I found this book well done and quite useful. I have worked in this realm for almost 40 years, and I still found new material to explore and consider. The depth of the research and documentation befits a subspecialty that is moving from infancy into adolescence. This textbook and others like it are sorely needed. HG

**—Scott Shannon, MD**
**Author, *Mental Health for the Whole Child***
**Fort Collins, Colorado**

***The Spirit of Tequila* by Joel Salcido. San Antonio, TX: Trinity University Press; 2017. Hardcover, 173 pages. ISBN: 978-1-59534-823-4. $29.95**.

Tequila is the most iconic liquor from Mexico. Named for the town of Tequila in the state of Jalisco, the spirit is distilled from the hearts (caudices, referred to as *piñas* in Spanish because of their pineapple- or pinecone-like shape) of the blue Weber agave (*Agave tequilana*, Asparagaceae) native to mineral-rich volcanic soils in the hillsides and valleys of the Sierra Madre Occidental. Distilled since the 1600s, tequila is now one of the most popular liquors in the United States. The first three barrels of tequila imported to the United States were shipped by Sauza through El Paso, Texas, in 1873. Import rates from Mexico to the United States have risen to about 33.2 million proof gallons in 2016.

The name "tequila," a type of alcohol called mescal, is now controlled by the Mexican government and refers to the distilled liquor made in or near the town of Tequila. Tequila is a protected name similar to "Bordeaux" for red wine or

"Champagne" for white sparkling wine produced in the regions of the same names in France.

Unlike some of the books published in the past decade about tequila, this book contains no recipes and minimal text about the actual history of the plant, its ethnobotany, and the power of the plant and its alcoholic products. It is a superbly artistic book with beautifully compelling photography of the region surrounding Tequila, the agave plant, historic artisanal distilleries, and field workers (*jimadores*) and their field animals: images that speak to the heart and soul of the region and its people. The book includes almost 90 photos, taken with a medium-format camera.

Author/photographer Salcido grew up in this region, spending his teenage years in the border town of El Paso (my hometown) and returning to his native Mexico time and again to capture the essence of its places, people, plants, and *pulque* products. (Pulque — the traditional precursor of the distillate tequila — is the alcoholic beverage made by fermenting, as opposed to distilling, *aguamiel*, the sap extracted from the live maguey [*A. americana*] or agave plant.)

The photos are stunningly alive: a virtual journey to a part of Mexico's heartland, where companies like Cuervo, Herradura, and Sauza have been producing tequila since 1758 (the year of the founding of Cuervo, the first company to begin the mass-distillation of tequila).

For tequila connoisseurs, ethnobotanists, herbalists, and others who may like to partake of a tequila shot or a margarita, this exceptional book is an artistically worthy addition to the documentation of an ancient cultural practice that produces one of the world's unique beverages. HG

**—Mark Blumenthal**
**ABC Founder and Executive Director**
**Austin, Texas**

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***Ethnopharmacology*** by Michael Heinrich and Anna K. Jäger, eds. Hoboken, NJ: John Wiley & Sons, Inc.; 2015. Hardcover, 462 pages. ISBN: 978-1-118-93074-8. $110.00.


*Ethnopharmacology* is part of a series of textbooks produced by the ULLA Consortium, a European academic collaboration in teaching and research of pharmaceutical sciences. ("ULLA" is derived from the first letters of the founding universities of Uppsala, Leiden, London, and Amsterdam.) As explained in the foreword, the main audience of the book is PhD and other postgraduate students in the fields of pharmacy and pharmaceutical sciences. Edited by Michael Heinrich, PhD, and Anna K. Jäger, PhD, the book contains 34 chapters, each written by experts in the field.

The book is separated into three sections, the first of which addresses the fundamental challenges of ethnopharmacological research. It starts with the meaning of the term "ethnopharmacology," which — as the reader will observe — is not as clear as it may seem. In the book's preface, 29 definitions of "ethnopharmacology" by various scholars are given, and a few additional explanations are found throughout the book. I liked the explanation by Elizabeth Williamson, PhD, for its simplicity: "Ethnopharmacology is the study of natural medicines used by people of different cultures, and how these medicines may work." There are, however, many other ways to explain what the discipline encompasses.

A number of other important aspects regarding the fundamental challenges of ethnopharmacology are brought up within the first section. Jäger reflects on the questions about the deliverables of ethnopharmacological research: Should it be new drug leads, or new herbal medicines? Is the goal to rationally explain the traditional uses of herbal medicines in the various cultures, or should the researchers strive to evaluate the efficacy, safety, and toxicology of traditional medicines in order to improve the local health care system?

Other chapters in this section discuss biodiversity and protection of medicinal plants in the wild and the intellectual property (IP) rights of the indigenous peoples who possess knowledge about medicinal plant use. Given the increaing popularity of many botanical medicines, and the fact that only a small number of medicinal plant species are cultivated, sustainable harvesting practices are crucial if herbal medicine is to be available for future generations. Two chapters by Vernon H. Heywood, PhD, and Geoffrey A. Cordell, PhD, respectively, suggest ways to alleviate pressure on plants that are threatened by overharvesting.

The legal challenges with IP rights for indigenous peoples are explained in chapters by Heinrich and Alan Hesketh, PhD, respectively. Questions about who owns the IP (which can be difficult to determine since the same plant may have similar uses among people from many cultures) and how and when the IP owners should be reimbursed are explored using a number of case studies. The chapters also discuss regional differences in relation to the legal situations, with some countries welcoming international collaboration and others enacting regulations that "prevent access by outside workers." The choice of authors from both academia and industry to write chapters on the IP topic is particularly

welcome, since these two sectors generally do not have the same approach to ethnopharmacological research and IP issues.

A great chapter in the first section is "The Anthropology of Ethnopharmacology," written by Ina Vandebroek, PhD, and Daniel E. Moerman, PhD. It shows that ethnopharmacology can be studied in rather unexpected places, such as in New York City, and that it is not restricted to the use of herbal medicine in past centuries, but that it is a dynamic field of research and very much alive in the 21st century. The authors also discuss the importance of the spiritual aspects of healing, and that the healing process not only involves physical symptoms, but also should address the mental aspects of the problem. This holistic approach to healing is often neglected when researchers attempt to transfer findings from the field into a laboratory.

The second section of the book includes chapters that summarize findings about specific pharmacological topics, such as antibacterial and antimalarial drug leads, botanicals for central nervous system disorders, respiratory conditions, inflammatory diseases, endocrine and urological problems, bone and joint health, and metabolic disorders. Most chapters contain a short introduction about the topic of interest and illustrate the importance of ethnopharmacological research with a small number of cases. Examples include arnica (*Arnica montana*, Asteraceae), devil's claw (*Harpagophytum procumbens*, Pedaliaceae), Chinese skullcap (*Scutellaria baicalensis*, Lamiaceae), cayenne (*Capsicum annuum*, syn. *C. frutescens*, Solanaceae) or turmeric (*Curcuma longa*, Zingiberaceae) as examples of anti-inflammatory medicines; or the use of marshmallow (*Althaea officinalis*, Malvaceae), echinacea (*Echinacea* spp., Asteraceae), ephedra (*Ephedra sinica*, Ephedraceae) or thyme (*Thymus vulgaris*, Lamiaceae) for respiratory conditions. On the other hand, some chapters detail long lists of plants used for a specific condition (e.g., plants used for bone and joint disorders, or plants used for wound healing in Ghana). The section also includes chapters on the marketing and clinical aspects of ethnopharmacological research.

The final section provides perspectives from around the globe, with chapters on ethnopharmacology in sub-Saharan Africa, India, China, Southeast Asia, Europe, the Eastern Mediterranean countries, the Middle East, Australia and Oceania, Central and South America, and Mexico. The section also contains an excellent chapter on the importance of processing ingredients used in traditional Chinese medicine. The authors, Ping Guo, PhD, Eric Brand, and Zhongzhen Zhao, PhD, emphasize the relevance of crude raw material processing and give examples of how differences in preparation, such as cutting, frying, steaming, and stewing of an herb, will lead to changes in its phytochemical profile that affect the efficacy and/or toxicity of an herb. This is another important aspect of ethnopharmacology that sometimes gets lost in translation from the field into the laboratory.

Some of the chapters have a very narrow focus, such as the overview on epidermal growth factor receptors and downstream signaling pathways as cancer treatment targets, the chapter on Ghanaian medicinal plants for wound healing, and the chapter on ethnopharmacology in elementary, primary, and secondary education. These chapters seem a bit of a mismatch with the general theme of the book. Overall, however, the book gives a good overview of ethnopharmacology and the overarching research topics that it encompasses. The convergence of anthropology, botany, chemistry, pharmacology, and medicine makes ethnopharmacology not only a fascinating area of research, but also a challenging one, since expertise in all these areas is required. The open and honest discussions about the challenges related to research in the field may be the most beneficial parts of the book for those who are considering or undertaking a career in academia, the principal audience of the book (although the difficulties to obtain funding to do such research are not mentioned). Even those who are not university researchers but who have a genuine interest in ethnopharmacology may find many of the chapters an interesting read. HG

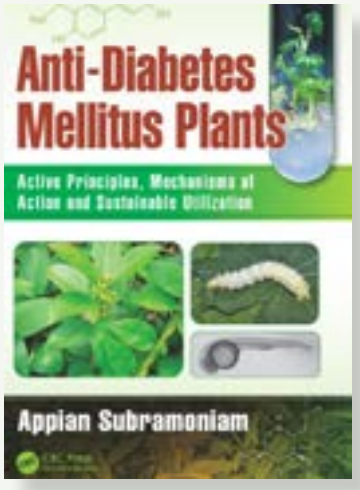
**—Stefan Gafner, PhD**
**ABC Chief Science Officer**
**Austin, Texas**

***Anti-Diabetes Mellitus Plants: Active Principles, Mechanisms of Action and Sustainable Utilization*** by Appian Subramoniam. Boca Raton, Florida: CRC Press; 2016. Hardcover, 390 pages. ISBN: 978-1-4987-5323-4. $119.95.

This book is a follow-up to *Plants with Anti-Diabetes Mellitus Properties* (CRC Press, 2016), a comprehensive collection and discussion of anti-diabetic plants. Here, Appian Subramoniam, PhD, focuses on the mechanisms of action of anti-diabetic plants and bioactive compounds therein. This work is thorough and includes diverse chapters describing aspects of diabetes and medicinal plant research, ranging from a physiological overview of the disease to sustainable use of anti-diabetic plants.

The book begins with an overview of the various causes of diabetes, with an emphasis on cellular abnormalities that lead to type 2 diabetes. Insulin signaling dysfunction resulting from overconsumption of both carbohydrates and fats, the role of autoimmunity in type 1 diabetes, and causes of circulatory problems in patients with diabetes are all discussed. Several helpful diagrams and figures illustrate the highlighted mechanisms. Also, prominent scientists associated with major insulin signaling and metabolic discoveries are appropriately cited.

Chapter 1 provides a comprehensive foundation for understanding how the plants and compounds therein alleviate symptoms of diabetes, and it serves this function well, overall. Nonetheless, a few things are odd here. Some basic terms, such as endothelial cells and nitric oxide synthase, could have been defined. These omissions result in some of the introduction getting too detailed without a sufficient framework. Contemporary therapeutics are defined, but in the discussion of metformin (although not a true botanically derived compound), no mention is made of its origin based on a compound found in goat's rue (*Galega officinalis*, Fabaceae). This is important, as this drug is one of the most widely used therapeutics for diabetes and provides strong justification for the investigation of medicinal plants as leads for new drug discovery.




Chapter 2 is mainly a list of plant compounds, their botanical origin, and brief descriptions of mechanisms of action and research highlights. This section is rather exhaustive and includes 303 compounds, but some of the entries are missing the compound classification (a very helpful feature in most of the entries), and the brief sections describing research are not as up-to-date or comprehensive as they could be. This can be overlooked, as the book's main goal is to encourage necessary research into potential botanical therapeutics; this makes for a broad perspective at the expense of some details.

Chapter 3, "Mechanism of Action of Anti-Diabetes Mellitus Plants," is especially strong. The main mechanisms of action are explained here with a focus on cellular regulation. There is an emphasis on clearly describing how bioactive plant compounds may act on various targets, such as insulin action and 5'-adenosine monophosphate-activated protein kinase (AMPK); this is a critical concept in diabetes research, because this chronic illness often disrupts multiple metabolic pathways. The author expands from here to include plants that exhibit the mechanisms of action introduced in the beginning of the chapter and examples of plants with numerous cellular targets. The diagrams here are helpful, concise and easy to understand. The chapter ends with a list of plants for which the anti-diabetic mechanism(s) remain unknown, illustrating potential research directions for those interested in pursuing them.

There is also a comprehensive chapter on herbal combinations, including definitions of synergistic and additive effects, with examples of the interaction of certain plant compounds and the resultant impact on bioactivity. Additional chapters address models for studying anti-diabetic activity (both in vivo and in vitro) and sustainable use of anti-diabetic plants. Those who are beginning anti-diabetic research or reviewing additional plants to work on will appreciate the thorough descriptions of models.

This book seems designed as a launch pad for ideas about pursuing anti-diabetic plant research and how to go about this. It makes a great laboratory reference for both students and senior researchers looking for new plant candidates and/or methodology for anti-diabetic research. The price of this book is fair, considering its comprehensive nature. I would highly recommend this book as a reference for those interested in research on the potential anti-diabetic activity of whole plants or plant-derived natural products. HG

**—Amy C. Keller, PhD**
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**Denver VA Medical Center**
**University of Colorado School of Medicine**
**Division of Endocrinology, Metabolism & Diabetes**
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# Judith 'Judi' Daye Wagner 1948-2017

Judith Wagner, a natural products pharmacist who was dedicated to providing her customers with herbal medicine guidance, died on September 29, 2017. In addition to her work with clients, Wagner was a wonderful mother and spectacular human being.

Wagner was born on September 19, 1948, and grew up in Baltimore, Maryland. She spent most of her life between Baltimore; Atlanta, Georgia; and Asheville, North Carolina. Wagner's career as a natural products pharmacist began early. During high school and college, she worked for her father at Charlie Wagner's Arcade Pharmacy in Baltimore. According to Wagner's daughter Miriah Lantz-Wagner, Judi would recommend a tea of lemon (*Citrus* × *limon*, Rutaceae), ginger (*Zingiber officinale*, Zingiberaceae), and honey for sore throats and coughs, rather than the pharmacy's best-selling cough syrup. Lantz-Wagner expects her mother would have lost her job had Charlie not thought so highly of her.

In 1970, Wagner graduated with a Bachelor of Science in education with honors and then, in 1977, a Bachelor of Science in pharmacy, both from the University of Maryland. A consummate advocate of natural health care, Wagner studied massage therapy between 1986 and 1991 and herbal medicine at the BotanoLogos School of Herbal Studies in Clayton, Georgia, under herbalist Patricia Kyritsi Howell. She was also a lifelong practitioner of yoga and an active member of the Georgia chapter of the American Herbalists Guild (AHG).

For almost 50 years, Wagner worked in various settings as a massage therapist or pharmacist, where she provided integrative pharmacy guidance to her customers. She researched potential natural therapies for those with AIDS before it was common to do so, and conversed with experts all over the country. In one pharmacy where Wagner worked, a customer credited her knowledge with saving his life when a drug he was prescribed depleted him of an essential mineral. She educated him on the critical importance of taking a supplement. Wagner also railed against what she considered the off-label misuse of conventional drugs, such as using medications to inhibit gastric acid production in infants with colic.

Wagner had a deep compassion for humanity that, according to her daughter, was inspired by the social justice work done by her parents and grandparents. Wagner carried on this legacy of social justice and passed it on to her children by taking them to peace marches and gay pride parades and being involved with AIDS ministry work and volunteering.

According to herbalist Patricia Howell, a former Council Member of the AHG:

> Besides being a steadfast friend to me and many, Judi embodied both the ability to understand science, in her case pharmacology, and, equally, the endless possibilities that herbs offer. She valued both and was generous in sharing information…. As an educator, here at BotanoLogos and other places, Judi advocated for the potential benefits herbal medicines had to offer. Judi broke down the mystique of drug therapies and honestly advocated for pharmaceuticals that offered what herbs could not, while at the same time emphasizing the lifestyle changes that were the real source of health and healing. She had a wry sense of humor, a curious mind, and deep intellect, along with the ability to savor life as she nourished her family, garden, and large circle of friends.

In addition to her work and family, Wagner loved gardening, hiking, medicine-making, knitting for friends and family, watching foreign movies, theater, dance, and travel. She is survived by her children Sky Lantz-Wagner, Spring (Josh) Taylor, and Miriah Lantz-Wagner; brother Jeff (Nancy) Wagner; partner Richard Silverstone; stepsons Gabe and David Silverstone; four grandchildren; and a niece and nephew. Her wonderfully smiling spirit is missed. Many thanks to Miriah for sharing part of Judi's family history, Judi's parents and grandparents for the wonderful values they imbued in her, and Judi's children for sharing a part of their mother with the herbal world. HG

**—Roy Upton, RH, DipAyu**
**President, American Herbal Pharmacopoeia**
**Scotts Valley, California**

Besides being a steadfast friend to me and many, Judi embodied both the ability to understand science, in her case pharmacology, and, equally, the endless possibilities that herbs offer.

# Tierney Salter
# 1957-2017

Tierney Salter, owner of The Herbalist store in Seattle, Washington, died on May 21, 2017, following complications with her lifelong battle with severe asthma. Due to her health condition, Salter turned to herbal medicine as a natural and sustainable way to alleviate her symptoms and improve her quality of life, and dedicated her career to helping others do the same. She opened The Herbalist in the Ravenna neighborhood of Seattle in 1984 and a second location in Seattle's Capitol Hill in 2014.

After earning a degree in anthropology from the University of California, Santa Barbara in 1980, Salter studied under the late herbalist Michael Moore at his Southwest School of Botanical Medicine in Santa Fe, New Mexico, from 1980 to 1982. She then moved to Seattle and opened The Herbalist.

According to Alison Brownrigg, who worked with Salter for 15 years at The Herbalist, Salter's experience with her own chronic illness inspired her to open the store (email, January 4, 2018). "The natural medicine industry was a very different place in 1984," Brownrigg wrote, "and, even in a progressive city like Seattle, she was definitely breaking boundaries and pushing people's ideas of self-care."

At The Herbalist, Salter sold her own line of products, including single-herb and combination-herb tinctures, salves, and teas, and used organic and wild-harvested materials whenever possible. Eventually, her line expanded to more than 200 products, and she added private label body care products and vitamins to her shelves. She kept up with the evolving regulatory landscape for natural products and steered her company through labeling concerns, scrutiny from the US Food and Drug Administration after the passage of the Dietary Supplement Health and Education Act in 1994, and pressure from increasing competition.

Salter also studied iridology, the practice of examining patterns, colors, and other characteristics of the iris to determine information about a patient's health, and offered in-store consultations. "She was very generous with her knowledge," Brownrigg noted. "She never had an employee sign a non-compete clause, she never hid her recipes, [and] she wasn't [upset] when a former employee became competition. [She was] genuinely happy for their success."

Salter "practiced what she preached" in regard to natural healing, and used her own products faithfully. She advocated for natural cleanses and integrated dietary suggestions into her recommendations and protocols. ("But she definitely enjoyed life and wine and good food," Brownrigg added.) She strived to make her shop a healing entity in and of itself, using aromatherapy and similar holistic techniques to create a soothing atmosphere. The shop's logo, a beaver with herbs in its mouth, held deep meaning for Salter. "Beavers make their homes with many different entrances and exits," Brownrigg recalled her mentor saying, "so they have lots of options in their lives, many ways to do things, and come and go as they please. She thought this was the way with healing: there are many different options to choose, including herbal medicine."

Brownrigg remembers Salter as intelligent, savvy, vibrant, and quick to laugh. She was devoted to her family, and her two sisters and son worked at her store. She also had a huge heart for animals, and often brought her dogs to work with her. She visited Mexico frequently, and maintained a residence there as well. "No article about her would be complete without a nod to her flair," Brownrigg wrote. She enjoyed a flamboyant personal style with bright colors, especially turquoise.

Tierney Salter is survived by her son Philip; sisters Erin Chesledon and Tracey Isaacson; and her nephew, uncles, and cousins. "All she would care about her legacy is that she helped people heal," Brownrigg concluded. "I really think that's what it was all about for her." HG

**—Hannah Bauman**

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

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

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## Mexican Prickly Poppy

***Argemone mexicana*, Papaveraceae**

Photograph taken by Eric Yarnell, ND
Captured with a Canon EOS Rebel T3i
Canon Ultrasonic Macro Lens EF 100 mm

The Mexican prickly poppy (*Argemone mexicana*, Papaveraceae) is an annual herb with thistle-like leaves and showy yellow flowers.[1] A native to the American continents, it has been naturalized throughout the Indian subcontinent and is known as *satyanashi* in the Ayurvedic materia medica.[1,2] Though the plant is toxic to animals, it is used in small doses for humans as a diuretic, purgative, and anthelmintic in Ayurveda.[2] The seeds are considered purgative; the roots are used as an anthelmintic and diuretic; and the juice from the stem is used for eye conditions such as ophthalmalgia and opaque corneas. The seeds resemble mustard (*Brassica juncea* and *B. nigra*, Brassicaceae) seeds, and prickly poppy seeds have been reported as adulterants of mustard seeds. The non-edible toxic seed oil can cause a serious condition known as epidemic dropsy (swelling of the body) when added to mustard seed oil.[3]

### References


1. Plant Database: *Argemone mexicana*. Lady Bird Johnson Wildflower Center website. January 3, 2018. Available at: www.wildflower.org/plants/result.php?id_plant=ARME4. Accessed January 26, 2018.
2. Oudhia P. Medicinal weed satyanashi (*Argemone mexicana* Linn). New Crop Fact Sheets: Purdue University; 2002. Available at: www.hort.purdue.edu/newcrop/CropFactSheets/argemone.html.. Accessed January 26, 2018.
3. Epidemic Dropsy (Information Sheet). WHO Regional Office for Southeast Asia website. [cached] May 22, 2002. Available at: https://web.archive.org/web/20060821215951/http://w3.whosea.org/techinfo/dropsy.htm. Accessed January 29, 2018.

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