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HERBALGRAM

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Goji Berry Profile

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dear *reader*

It has been many years since our good friend Christopher Hobbs, PhD, has contributed an extensive article to these pages. His literature reviews for *HerbalGram* in the late 1980s and early 1990s explored the emerging science on a host of up-and-coming herbs: sarsaparilla, St. John's wort, feverfew, valerian, and hawthorn. In fact, *HerbalGram* issue 18/19, the first (double) issue published in the fall of 1988 under the auspices of the just-established ABC, carried a three-color drawing of St. John's wort and Hobbs' extensive monograph on this herb. Ten years later, St. John's wort would become a widely popular herb, and it was featured on the cover of *TIME* magazine in November 1998. Hobbs' articles helped these herbs gain interest and popularity, and were some of the very first scientific reviews of these herbs published in the United States.

Since then, Hobbs, a fourth-generation herbalist, and an author, botanist, and accredited acupuncturist, has earned a doctorate at the University of California, Berkeley. His extensive cover article, which reviews some of the key chemical, biological, and quality control aspects of fungal mycelia and fruiting bodies, will no doubt become a seminal article on this fascinating and increasingly popular area of "herbal medicine" (the term is not strictly accurate as fungi are not "herbs"; they occupy their own biological kingdom).

Our herb profile this issue is on lycium fruit, popularly known as goji berry. The article, by ABC's Gayle Engels and Traditional Medicinals' Josef Brinckmann, includes an array of information on the small but highly interesting medicinal Asian fruits, most of which come from China.

Uncritical coverage by mainstream media of research on herbs and conventional foods continues to confuse the public regarding the relative benefits and risks of many ingredients, both popular and obscure. In this issue, ABC Chief Science Officer Stefan Gafner, PhD, contributes a Research Review on the confusion created by a clinical trial and accompanying editorial published in the *Journal of the American Medical Association*, and by resulting media coverage. The clinical trial was conducted using a proprietary cranberry extract and, in the view of Gafner and numerous others, it included a set of patients that was not appropriate for measuring the effectiveness of the extract. As Gafner explains, the trial was not designed to measure cranberry's well-demonstrated *preventive effect* for urinary tract infections.

HerbalGram Assistant Editor Connor Yearsley contributes an article on the National Animal Supplement Council, a trade association of providers of supplements designed for use by companion animals: dogs, cats, and horses. There is significant and continued growth in this market segment. Supplements for animals are regulated by the US Food and Drug Administration as either foods or drugs, but there is no specific legal category for animal supplements. Thus, marketers of these supplements are not legally allowed to make certain claims regarding the potential therapeutic benefits of these products. Of particular concern to the NASC is ensuring the proper identity and purity of ingredients used in animal supplements. The organization has developed a fairly sophisticated system of self-regulation for qualifying contract manufacturers, suppliers of raw materials, and other service providers along the animal supplement suppy chain. This gives NASC members the ability to properly qualify suppliers and ingredients in a data sharing modality, thereby reducing costs that might otherwise be too great.

Speaking of quality control, in this issue we announce the completion and release of two more publications as part of the ABC-AHP-NCNPR Botanical Adulterants Program's continuing efforts to educate members of the herb and dietary supplement industry about herbs with confirmed reports of intentional or accidental adulteration with lower cost, foreign material. We have recently published Botanical Adulterants Bulletins on the adulteration of saw palmetto extracts with vegetable oils and of St. John's wort extracts with related species and food dyes.

Finally, we welcome 12 medicinal plant experts as new members of the ABC Advisory Board. As an indicator of the global reach of scientific research and the expanded scope and role of ABC, five of these 12 new members are from outside the United States. In addition, at least five are experts in medicinal plant analysis and quality control, which reflects ABC's continued efforts to report on and help ensure appropriate quality of botanical materials used in consumer products. HG

Mark Blumenthal

ABC Advisory Board

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

HERBALGRAM
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Shiitake *Lentinula edodes*
Photo ©2017 Steven Foster

departments

On the Cover
Shiitake *Lentinula edodes*
Photo ©2017 Steven Foster

Errata

In issue 112, there was an inaccurate statement on page 50 regarding US poison center calls related to kratom exposure from January 2010 through December 2015. Of the calls, 64.8% involved kratom used *in isolation*, not with other substances, as was written.

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Lycium (Goji Berry)

Lycium barbarum* and *L. chinense

Family: Solanaceae

INTRODUCTION

The plant genus *Lycium* contains approximately 80 species distributed in Asia, South America, southern Africa, and, less commonly, temperate Europe.[1] Of the seven species that grow in China, the two primary medicinal species are *L. barbarum* and *L. chinense*, which are used interchangeably in traditional Chinese medicine (TCM),[2] traditional Japanese Kampo medicine,[3] and traditional Korean medicine.[4] *Lycium chinense* also occurs in parts of Japan (including the Ryukyu Islands) and Korea (including Jindo Island).[1,5]

Both *L. barbarum* and *L. chinense* are deciduous shrubs, usually thorny, with arching or prostrate branches and alternate, lanceolate, gray-green (*L. barbarum*) or bright green (*L. chinense*) leaves. *Lycium barbarum* can grow to a height of almost 10 feet (3 meters) while *L. chinense* can grow slightly larger. *Lycium barbarum* has five-lobed flowers that have been described as pale rose, violet, or light purple in color, and *L. chinense* has flowers that are purple.[6,7] From June through September, these species produce oval red fruits that are tangy yet sweet and approximately one inch (2.5 centimeters) long.[6,8]

The berries are harvested when ripe, dried until the pericarp is shrunken, then exposed to strong sunlight until the exocarp is dried and hard, but the inner pulp is still soft. The dried root bark of both species is also used in TCM.[9] Since the fruits of the two species of lycium discussed in this article are used interchangeably in TCM, attributed uses apply to both species unless stated otherwise. This article focuses mainly on lycium fruit, although use of lycium root bark in TCM may be mentioned in context.

In the United States, the preferred standardized common name for both *L. barbarum* and *L. chinense* is simply

Lycium *Lycium chinense*
Photo ©2017 Steven Foster

"lycium," according to the second edition of the American Herbal Products Association's (AHPA's) *Herbs of Commerce*. *Lycium barbarum* is also known as barbary wolfberry, and *L. chinense* is sometimes referred to as Chinese wolfberry. In the US market, lycium fruit is known as goji berry, an Americanized spelling of *gou qi zi*, the Chinese pinyin transliteration of 枸杞子. In Japan, lycium fruit is known as クコシ (*ku ko shi*) and, in Korea, it is known as 구기자 (*gu gi ja* or *ku gi cha*).[10]

While *L. chinense* is referred to simply as *gou qi*, *L. barbarum* is referred to with qualifiers, such as *ning xia gou qi*, which refers to the Ningxia Hui autonomous region from where most of the supply originates. The variety *L. barbarum* var. *barbarum* is widely cultivated, especially in Ningxia, but also in the city of Tianjin.[1] Bensky et al. (2004) describe three different regional types of lycium fruit grown in China: western lycium fruit (*xi gou qi zi*) from Ningxia, Gansu province, and Qinghai province; Tianjin lycium fruit (*jin gou qi zi*) from Tianjin; and local lycium fruit (*tu gou qi zi*), also called mountain lycium fruit (*shan gou qi zi*), which is wild-collected in Henan province.[11] Recently, metabolic profiling methods have been used to differentiate geographical origins of lycium fruit samples from China, Mongolia, and Tibet.[12] Additionally, fruits of *L. barbarum* and *L. chinense* from different regions can be distinguished based on a combination of taste pattern, Brix percentage (sucrose content), betaine, and saccharide composition analyses.[5]

Ningxia lycium that is traditionally harvested and processed is a protected geographical indication (PGI) product. When produced in compliance with the PGI standard ("GB/T 19742-2008: Product of geographical indication – Ningxia lycium"), geo-authentic lycium fruit may be labeled and marketed with the PGI certification mark issued by China's General Administration of Quality Supervision, Inspection and Quarantine.[13]

Nearly all of the global commercial supply of lycium fruit is obtained from both wild-collection and cultivation in China,[14,15] mainly in northern to northwestern areas, especially Qinghai province and the Ningxia and Xinjiang Uygur autonomous regions, but also Gansu and Shaanxi provinces and the Inner Mongolia and Xizang (Tibet) autonomous regions.[10] Although China is the only major user, producer, and exporter of lycium fruit in the global market, China also occasionally imports very small amounts from South Korea and North Korea.[16] South Korea produces *L. chinense* fruits in the provinces of South Chungcheong and South Jeolla.[5] Three varieties of *L. chinense* were developed and released in South Korea between 1997 and 2000 with improved yield, insect resistance, and saponin content: "Cheongyang Kugija" (1997), "Bulro Kugija" (2000), and "Cheongdae Kugija" (2000).[17] Most of the certified organic goji berry (both farmed and wild-harvested) in the global market originates from Qinghai province and the Ningxia autonomous region in China, but some organic production also takes place in Gansu, Liaoning, Shaanxi, and Tianjin provinces, and the Inner Mongolia and Tibet autonomous regions.[18] Although there are popular goji products labeled as "Himalayan," the term "Himalayan goji" is only for marketing purposes and is not an actual geographical indication.

Hundreds of years ago, *L. barbarum* was introduced into other parts of Asia and parts of Europe. The first known record of *L. barbarum* cultivation in Europe, in what is now the Czech Republic, dates back to 1785. Having escaped cultivation, it was first reported as growing wild there in 1870, and is now considered invasive with an observed impact on native biodiversity.[19] Classified as a non-native invasive species in the Danube Delta region of Romania,[20] *L. barbarum* is also reportedly encroaching on disturbed kurgans (ancient burial mounds) in the steppe zone in parts of Eurasia from the Danube Delta to Mongolia.[21] One of the authors of this article (JB) has seen large *L. barbarum* plantations surrounding stone-slab tombs in the Gobi Desert.

HISTORY AND CULTURAL SIGNIFICANCE

The origin of the common name wolfberry corresponds to the Chinese name *gou qi zi*, as the character for *gou* means dog or wolf, and the character for *zi* means small

fruit.[22] The genus name *Lycium* appeared in 1737 with the synonym *Jasminoides* in the first edition of *Genera Plantarum* by Swedish botanist Carl Linnaeus (1707-1778).[23] Today, *Jasminoides flaccidum* is listed as a synonym of the currently accepted name *Lycium barbarum* while *J. rhombifolium* is listed as a synonym of *L. chinense*.[24] The species *L. barbarum* was named in 1753 by Linnaeus in his *Species Plantarum*.[25] The species name *barbarum,* the neuter gender of *barbarus*, stems from the ancient Greek word for foreign or barbarous.[26] *Lycium chinense* was named in 1768 by Philip Miller (1691-1771), a Scottish horticulturalist and Chelsea Physic Garden (London) botanist, in the eighth edition of *The Gardeners Dictionary*.[27]

Lycium fruit was first described in the premodern classic *Shen Nong Ben Cao Jing*, the *Divine Farmer's Classic of Materia Medica*, compiled in the first century CE.[28] Its medical use was later recorded in the third century CE text *Ming Yi Bie Lu*, the *Miscellaneous Records of Famous Physicians*[29] (also translated as *Informal Records of Eminent Physicians*), an anonymous work that, according to Hsu and Harris (2012), has been erroneously attributed by other authors to Daoist physician Tao Hongjing (456-536 CE).[30] According to Dharmananda (2007), the use of lycium fruit "in traditional formulas was rather limited until the end of the Ming Dynasty period (1368–1644)" when it was often combined with tonic substances in formulas indicated to "nourish the kidney."[22] According to an English translation of the 1970 *Official Chinese Paramedical Manual*, lycium fruit acts to strengthen the kidney meridian, restore semen, nourish the liver meridian, and clear vision.[31]

Additional uses in TCM include addressing diabetes, vertigo, nocturnal emissions, consumptive cough, problems with the loins and knees, sore back and legs, mild abdominal pain, infertility, prematurely gray hair, night sweats, diminished visual acuity, thirst, and wasting.[29,32,33]

Since lycium is an important medicinal plant widely used in the Asian systems of medicine, quality standards monographs that provide specifications and test methods for the fruit have been published in the *Japanese Pharmacopoeia*,[3] *Korean Pharmacopoeia*,[4] *Pharmacopoeia of the People's Republic of China*,[9] and *Taiwan Herbal Pharmacopoeia*.[2] A quality standards monograph for "Barbary Wolfberry Fruit" first entered the *European Pharmacopoeia* (PhEur) in the fourth supplement to the eighth edition (PhEur 8.4) in April 2015, and remains official up through the current ninth edition published in July 2016.[34] The US Pharmacopeial Convention proposed the development of a "Lycium barbarum Fruit" monograph for its *Herbal Medicines Compendium* in May 2013. A draft version of that monograph is available online with a call for submission of validated information needed to complete the monograph.[35]

CURRENT AUTHORIZED USES IN COSMETICS, FOODS, AND MEDICINES

In Asian countries where traditional Chinese, Korean, and/or Japanese medicine are practiced, as well as in some Western countries where TCM is recognized, lycium fruit is used as an active substance indicated for general debility with deficiency of vital essence manifested by aching of the loins and knees, dizziness, and tinnitus. Additional indications include anemia, impaired vision, and diabetes caused by internal heat.[9] Presently, in the United States, most states and the District of Columbia permit the practice of Oriental medicine with varying limitations on the scope of practice. In states where TCM formulations can be dispensed to patients, lycium fruit (or fruit extract) may be used as a component of herbal prescriptions for at-home preparation (by traditional decoction) by patients, or as a component of Chinese patented medicines, professional products, or practitioners' formulations dispensed by compounding pharmacies.[36]

Lycium fruit may also be used as a component of herbal dietary supplement products widely available outside of clinical practice in the United States.[37] While not expressly listed as Generally Recognized as Safe (GRAS) by the US Food and Drug Administration (FDA) for use in conventional food products, "goji berry" (*L. barbarum* only) is accepted as a food because the Environmental Protection Agency (EPA) has established tolerances for pesticides that may be used when it is cultivated as a food crop, per its inclusion in the EPA's "Crop subgroup 8–10A. Tomato subgroup." (This subgroup also includes other fruits in the Solanaceae family, such as capsicum [*Capsicum annuum*], eggplant [*Solanum melongena*], and tomato [*Solanum lycopersicum*], among others.) This means that certain chemicals (e.g., the fungicide azoxystrobin and the molluscicide metaldehyde) are approved for application to goji berry food crops in the United States.[38]

In Canada, lycium fruit is regulated as an active ingredient of licensed natural health products (NHPs, a category of drugs), which require pre-marketing authorization from the Natural and Non-prescription Health Products Directorate (NNHPD). "Fructus Lycii" is listed in Table 1 (General Medicinal Ingredients) of the "Natural Health Product: Traditional Chinese Medicinal Ingredients" monograph. Labels of licensed NHPs that contain preparations of pharmacopeial-quality lycium fruit may carry claim statements consistent with the indications for use provided in the *Pharmacopoeia of the People's Republic of China*.[39] Additionally, *L. barbarum* fruit is listed in Appendix 3 (Other Medicinal Ingredients) of the "Natural Health Product: Antioxidants" monograph. At the specified dosage equivalent (6 g dry), licensed *L. barbarum* fruit NHPs may be marketed with antioxidant claim statements (i.e., "source of antioxidants that help protect against cell damage caused by free radicals").[40] At the time of this writing (December 2016), there were 671 licensed NHPs that list "Lycium barbarum" as an ingredient, of which 624 list it as a medicinal ingredient and 47 as a non-medicinal ingredient; 114 licensed NHPs list "Lycium chinense" as an ingredient, of which 107 list it as a medicinal ingredient and seven as a non-medicinal ingredient; 40 licensed NHPs list "goji berry" as a non-medicinal ingredient; and seven licensed NHPs list "Fructus Lycii," of which two list it as the active ingredient.[41]

For herbal medicinal product companies in the European Union (EU), or in non-EU countries where the PhEur is an official compendium (e.g., Australia and Canada), the quality standards monograph established by the European Directorate for the Quality of Medicines (EDQM) for "Barbary Wolfberry Fruit – Lycii Fructus" (the dried, whole, ripe fruit of *L. barbarum*) can be used as the basis for active ingredient specifications.[42] Barbary wolfberry fruit is one of a total of 43 TCM herbal drugs that had been adopted in the eighth edition of the PhEur,[43] and this increased to 66 monographs in the ninth edition (De-An Guo email to T. Smith, January 20, 2017). The European Medicines Agency (EMA), however, has not yet developed a corresponding labeling standards monograph for statements that can be made on labels of registered traditional herbal medicinal products (THMPs) containing barbary wolfberry fruit.[44]

For use in cosmetic products, the European Commission's Health and Consumers Directorate lists "Hydrolyzed Lycium Barbarum Fruit" (hydrolysate of the fruit of *L. barbarum* derived by acid, enzymes, or another method of hydrolysis) and "Lycium Barbarum Amino Acids" (mixture of amino acids derived by the complete hydrolysis of the protein isolated from the whole plant) for skin-conditioning function, and lists "Hydrolyzed Lycium Barbarum Fruit Extract" for antioxidant and skin-protecting functions. "Lycium Barbarum Fruit Extract" is listed for antioxidant, hair-conditioning, and skin-conditioning functions. "Lycium Chinense Fruit Extract" is listed for antioxidant function, "Lycium Chinense Fruit Juice" (juice expressed from the fruit of *L. chinense*) for skin-conditioning function, and "Lycium Chinense Fruit Water" (aqueous solution of the steam distillates obtained from the fruit of *L. chinense*) for flavoring, masking, perfuming, and skin-conditioning functions.[45]

MODERN RESEARCH

Dried lycium fruits contain pyrrole alkaloids, hydroxycinnamic acids (e.g., chlorogenic acid),[46] carotenoids (e.g., zeaxanthin and β-carotene),[47,48] polysaccharides,[46] cerebrosides, glycolipids,[49,50] peptides,[49] flavonoids (e.g., kaempferol, myricetin, and quercetin),[48] triterpenes (e.g., β-sitosterol),[50,51] and amino acids (proline, taurine, γ-aminobutyric acid, and betaine),[48,52] as well as vitamins, such as ascorbic acid, riboflavin, and thiamin.[48] *Lycium barbarum* contains certain polysaccharides (*L. barbarum* polysaccharides or LBPs) that some studies suggest are the main bioactive constituents.[8,46,53,54]

In vitro and in vivo studies have shown lycium fruit to be anti-inflammatory,[55] antioxidant,[56,57] antifibrotic,[58] antiaging,[59] apoptotic,[60] cerebrovascular protective,[61] hepatopro-

Lycium *Lycium chinense*
Photo ©2017 Steven Foster

Human clinical trials have addressed diabetes, immune health, antioxidant effects, vision (specifically AMD), metabolic rate, weight and waist circumference, general wellbeing, fatigue, and stress.

tective,[58,59,62] hypolipidemic,[63] hypotensive,[59,62] hypoglycemic,[59,62-64] immunomodulating,[65] and neuroprotective.[66-71] Laboratory studies have also shown that lycium can cause cancer cell death (apoptosis),[72,73] inhibit growth of human breast cancer cells,[74] ameliorate physical fatigue,[75] improve insulin resistance,[76] reduce chemotherapy-induced hair loss,[77] protect against oxidative stress,[78-80] prevent prenatal stress-induced cognitive impairment,[81] protect against acetaminophen-induced acute hepatotoxicity,[82] treat age-related macular degeneration (AMD),[83] and significantly lower fasting blood glucose, total cholesterol, and triglycerides.[64,84] As one peer reviewer of this article noted, these research findings "do not necessarily translate to clinical results from consuming ordinary amounts of the whole fruits, their tea, juice, or commercial extracts." Such research may, however, suggest the "possible use of isolated components of lycium fruit and possible mechanisms of action for reported clinical benefits."

Human clinical trials have focused on *L. barbarum* and LBPs, and have addressed diabetes, immune health, antioxidant effects, vision (specifically AMD), metabolic rate, weight and waist circumference, general wellbeing, fatigue, and stress. As with all clinical trials of herbal products, various factors should be taken into consideration when interpreting the results. The CONSORT statement for herbal medicine interventions outlines many of these considerations (e.g., methodological quality, appropriate description of herbal intervention, potential conflicts of interest, etc.).[85] As indicated in the study summaries below, many of the tested LBP preparations lacked detailed characterizations by the authors. Additionally, many of the human trials summarized below have various design limitations that weaken their conclusions.

LBPs have been used in Chinese medicine to address various symptoms associated with type 2 diabetes, including excessive thirst and urination. A prospective, randomized, double-blind, controlled study of 67 patients who had been diagnosed with type 2 diabetes less than five years before the study examined the effects of LBPs on two other factors: postprandial glucose and lipid levels. Patients were given either 300 mg of LBPs (produced by a pharmaceutical company in Shanghai from fruit purchased from the Ningxia autonomous region; no additional information provided) or placebo in two doses per day for three months. Patients were asked to continue their normal therapy during the intervention period and had regular follow-up visits every two weeks. The oral metabolic tolerance test (OMTT) showed that the LBP group experienced a significant reduction in serum glucose and increase in high-density lipoprotein (HDL) levels after intervention, compared to baseline. The hypoglycemic effects were more significant in patients not taking hypoglycemic medicines than in those who were.[86]

At least five studies have been published on the positive effects of a 120-mL daily serving of *L. barbarum* juice standardized to supply an LBP equivalent of at least 150 g of fresh fruit (GoChi; FreeLife International Inc.; Phoenix, Arizona). The first, in 2008, was a randomized, double-blind, placebo-controlled (RDBPC) trial in which 34 healthy volunteers took either 120 mL of GoChi or placebo each day for 14 days. Subjects were instructed to discontinue use of *L. barbarum* and *L. barbarum*-containing foods, as well as dietary supplements, energy drinks, and green tea (*Camellia sinensis*, Theaceae) throughout the study. Subjects received a medical exam and their physical measurements were assessed (i.e., parametric data such as body weight, body mass index [BMI], blood pressure, heart rate, etc.), as well as their history of smoking, diseases, and dietary habits. While there were no significant changes in parametric data between days one and 15 in either group, the GoChi group experienced significant improvements in athletic performance, calmness, focus on activities, sleep quality, and feelings of contentment, happiness, and good health, compared to baseline. The GoChi group also experienced a tendency toward increased energy level and mental acuity, and had a significant reduction in feelings of fatigue and stress, compared to baseline.[87]

In a 2009 RDBPC study, 60 healthy, older Chinese adults (55 to 72 years old) were randomly assigned to take 120 mL of GoChi or placebo once daily for 30 days. Each subject received a medical exam, had physical measurements assessed (body weight, blood pressure, pulse rate, abdominal B-ultrasound, electrocardiogram, and chest X-ray), and provided background information that included disease history. Subjects had no acute diseases, took no long-term medications, and had no history of using GoChi. Subjects were instructed to discontinue use of *L. barbarum* and *L. barbarum*-containing foods at least two months prior to and throughout the study. Subjects were monitored to assure compliance. Both the GoChi and placebo groups experienced minimal changes in parametric data. However, significantly more subjects in the GoChi group (more than 60%) communicated increased ratings of general well-being compared to those in the placebo group (20%). While it was not statistically significant, the GoChi group also showed a tendency toward improved short-term memory and focus between the beginning and end of the study. Additionally, lymphocyte numbers and certain immunological markers (IL-2 and IgC) were significantly increased in the GoChi group, compared to baseline, which suggests that GoChi may have immunomodulatory effects.[88]

Another 2009 article, which resulted from the study discussed above, reported on GoChi's serum antioxidant effects. It was ascertained before testing that subjects in the GoChi and placebo groups had similar serum levels of superoxide dismutase (SOD), glutathione peroxidase (GSH-Px), and lipid peroxidation, as indicated by decreased levels of malondialdehyde (MDA). After 30 days of intervention, both SOD and GSH-Px had significantly increased (by 8.4% and 9.9%, respectively) and MDA had significantly decreased (by 8.7%) in the GoChi group. No significant changes were seen in the placebo group. This would suggest that GoChi has a positive antioxidant effect on humans and that use beyond 30 days might provide protection against free radical-induced conditions, such as coronary artery and neurodegenerative diseases.[89]

A 2011 article reported on two small RDBPC studies: one examined GoChi's effect on resting metabolic rate (RMR) and postprandial energy expenditure (PPEE), and the other looked at its effect on waist circumference and other morphometrics (BMI, waist circumference, and total body fat). Participants were recruited separately for the two studies and included healthy men and women with no evidence of heart, kidney, liver, or lung diseases. All participants completed a minimum two-week washout period during which they took no *L. barbarum* or *L. barbarum*-containing foods, and no dietary supplements, energy drinks, or caffeinated drinks, including green tea. During both studies, participants were monitored to ensure compliance. Results of these two studies, as described below, suggest that GoChi may stimulate metabolic rate, which may lead to a decrease in waist circumference.[90]

In the first study, eight subjects were randomly assigned to take a 120-mL serving of a placebo beverage or GoChi (containing one of three doses [30, 60, or 120 mL] of *L. barbarum*), along with a nutritional beverage to stabilize RMR for the four-hour test period. RMR and PPEE were measured by breath oxygen volume (VO_2; mL/min) before intake, and at one, two, and four hours after intake. One week later, the procedure was repeated by each group. All dosages of GoChi and placebo increased RMR over baseline. At one hour after intake, VO_2 measurement for 120 mL of GoChi increased by 58.26 ± 5.72 mL/min from baseline and was significantly higher than the placebo group, which increased by 24.58 ± 4.04 mL/min from baseline. At four hours after intake, VO_2 levels had returned to baseline for those in the placebo group and for those taking all dosages except 120 mL of GoChi. For those taking 120 mL of GoChi, VO_2 remained significantly higher than the levels achieved by other doses or placebo.[90]

In the second study, 33 healthy subjects consumed 120 mL (90 mL at breakfast and 30 mL at bedtime) of GoChi or placebo for 14 days. Caloric intake was restricted to 1,200 kcal during the intervention in both groups, and

subjects took daily 15-minute walks and recorded daily steps using pedometers. Waist circumference in the GoChi group decreased significantly mid-intervention and post-intervention compared to baseline. On day 15, it had been reduced by 5.54 ± 0.65 cm compared to pre-intervention. In contrast, in the placebo group, waist circumference on day 15 had been reduced by only 0.88 ± 0.83 cm, which was not a significant change from pre-intervention. Body weight, BMI, and total body fat did not change significantly in either group.[90]

A 2012 RDBPC study explored the effect of GoChi on general well-being and fatigue. After a two- to four-week washout period during which subjects discontinued use of energy drinks, caffeinated drinks, and *L. barbarum* or *L. barbarum*-containing foods, 39 healthy volunteers were randomly assigned to consume either 120 mL of GoChi or placebo in the morning every day for 30 days. Subjects were monitored for compliance. Participants also maintained a daily dietary diary and completed a short, intense exercise challenge on the first and last days of the intervention. Plasma levels of the adrenal steroids dehydroepiandrosterone (DHEA) and cortisol — which regulate numerous cardiovascular, homeostatic, immunologic, and metabolic functions — as well as glucose, blood urea nitrogen (BUN), and lactic acid were measured following the exercise challenge both pre- and post-intervention. While DHEA, cortisol, and lactic acid were increased significantly by the exercise challenge prior to the intervention in both groups, the GoChi group experienced significantly reduced DHEA and cortisol levels post-intervention compared to baseline. Glucose and BUN were not altered, and lactic acid levels were comparable in both groups. Additionally, while there were no significant changes in either group with regard to body weight or BMI, the GoChi group reported significant reductions in feelings of tiredness after exercise and improvements in circulation and general overall health, compared to placebo. This study suggests that the consumption of *L. barbarum* may promote adaptability to physical stressors (e.g., exercise), perhaps by limiting production and function of glucocorticoids, or by accelerating their metabolism.[91]

Zeaxanthin is an oxygenated carotenoid concentrated in the fovea (a small depression in the retina where visual acuity is greatest) and is one of the constituents of macular pigment. AMD, the thinning of the macular pigment that often occurs with age, is associated with loss of vision.[92] Because zeaxanthin dipalmitate is the most abundant carotenoid in *L. barbarum* (3,011-9,417 mg/g in certain genotypes),[46] its antioxidant properties are being studied for their role in protecting vision, specifically in cases of AMD.

A single-blind, placebo-controlled parallel trial published in 2005 investigated how fasting plasma zeaxanthin concentration changed with *L. barbarum* dietary supplementation over 28 days. Heat-dried *L. barbarum* berries (Rich Nature Goji Berries; Rich Nature Nutraceutical Labs Inc.; Mukilteo, Washington) were extracted, and the total zeaxanthin content was estimated by HPLC to be 194 mg/g, which suggested that taking 15 grams per day of the dried berries would provide additional dietary intake of 3 mg per day of zeaxanthin. Fourteen healthy subjects softened 15 grams per day in one cup of boiling water for 15 minutes after dinner, mashed the berries, then ingested them with the water. The control group drank a cup of plain warm water. Fasting blood samples were taken at baseline and at 28 days and assessed for zeaxanthin and lutein. At day 28, while plasma lutein levels had not changed significantly, there was a significant increase in both total and lipid-standardized plasma zeaxanthin in the test group, compared to baseline. The authors conclude that the benefits of lycium supplementation are strong but that longer-term supplementation studies are needed to determine if lycium berries can increase macular pigment density and protect vision in the aging population.[92]

Published in 2011, a RDBPC study evaluated the effects of a proprietary milk-based *L. barbarum* product on macular characteristics and plasma antioxidant levels in healthy elderly Chinese subjects over a 90-day period. Subjects were screened for terminal and significant chronic diseases, deteriorating health, glaucoma, cataracts, and lactose intolerance. Eligible subjects (N = 150, of which 133 completed the study) were randomly assigned to consume 13.7 g of Lacto-Wolfberry (LWB; Nestle R&D Centre Shanghai; Shanghai, China) — a product containing 530 mg/g *L. barbarum* fruit, 290 mg/g skim milk, 180 mg/g maltodextrin, 476 mg/g sucrose, and 34 mg/g colorants (providing 0.73 mg/g [10 mg per day] lycium-derived zeaxanthin and 5 mg/g [68.5 mg per day] lycium-derived vitamin C precursor) — or placebo with 200 mL of soup or hot water each day at lunch under supervision. Before and after intervention, detailed ophthalmic examinations of each subject assessed macular pigmentation and soft drusen count (a risk indicator for AMD) in the macula, and fasting blood samples assessed plasma zeaxanthin and total antioxidant capacity. Compared to baseline, there were no significant macular pigmentation changes in the LWB group, but 13 subjects in the placebo group showed progressive macular hypopigmentation ($P < 0.001$), and, at day 90, LWB subjects had significantly less macular hypopigmentation ($P < 0.01$). Also, while no subjects in either group had more than one soft drusen at baseline, eight people in the placebo group had a significant increase in soft drusen at 90 days, compared to no increase in the LWB group. With regard to plasma zeaxanthin and antioxidant capacity, both were stable over time in the placebo group but increased significantly in the LWB group (26% increase and 57% increase, respectively). The authors conclude that, while LWB consumption for 90 days can increase plasma zeaxanthin and total antioxidant levels and protect the macula of elderly subjects from hypopigmentation and the accumulation of soft drusen, the mechanism of action is unclear.[93]

FUTURE OUTLOOK

There are no known comprehensive reports available on the conservation status of wild *L. barbarum* or *L. chinense* in their East Asian native habitat.

China is the largest producer, user, and exporter of lycium fruit, having exported about 9.304 million kg in 2013, of which nearly half, or at least 4.538 million kg, was certified organic (including farmed and organic wild).[15] The total annual export volume is increasing significantly, up from 5.823 million kg exported in 2009. The main importers of Chinese origin lycium fruit in terms of volume are Hong Kong, Taiwan, Malaysia, the United States, the Netherlands, Vietnam, South Korea, Germany, Spain, the United Kingdom, and Japan.[10,16] China's 2015 harvest total was estimated to be more than 200 million kg,[94] which indicates that domestic consumption for use in TCM prescriptions, as well as for manufacture of value-added processed forms (e.g., extracts, juices, and wines) is significantly greater than the export market.

Market prices are impacted by geographical origin specifications (e.g., geo-authentic Ningxia lycium PGI), quality (food-grade or pharmacopeial-grade), color, and size grading. Lycium fruits are sized in "grains (berries) per 50 grams." The larger the berries, the fewer grains per 50 g and the higher the price. Several size grades are traded from 180 grains per 50 g up to 750 grains per 50 g, but the most frequently traded grades are 220, 280, and 380 grains per 50 g. At the time of this writing (December 2016), farm gate* prices were relatively stable with 280-grade berries of both Ningxia and Qinghai origin selling at 45-46 Chinese Yuan Renminbi (CNY) per kg ($6.76-$6.91 per kg); 220-grade from Qinghai at 48-50 CNY per kg ($7.21-$7.51 per kg); and 220-grade from Ningxia at 55 CNY per kg ($8.26 per kg).[95] At the same time, the indicative market prices† for 280-grade lycium berries ranged from 60-68 CNY per kg ($9.00-$10.21 per kg) at the major TCM markets in China.[96]

The use of lycium fruit (or fruit extract) as an active ingredient of traditional Asian medicines and of herbal dietary supplements and functional foods has been increasing significantly over the past few years. Given that China is the top producer and exporter for the global market and that nearly half of the export volume is certified organic, there is evidence that sustainable agriculture and sustainable wild-collection standards are being implemented in order to satisfy the growing demand. HG

—Gayle Engels and Josef Brinckmann

* The farm gate price refers to the dollar value of the produce paid directly to the producer (farming or wild-collection operation).

† The indicative market price refers to the dollar value of the produce paid to traders at the major TCM raw materials markets.

Lycium *Lycium chinense*
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ADOPT-AN-HERB

HerbMedPro™ PROGRAM

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

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.

AMERICAN BOTANICAL COUNCIL
SINCE 1988

Herbal Adopters

neem BIOTECH	**Garlic** *Allium sativum*
	Artichoke *Cynara scolymus*
Nature's Gift	**Helichrysum** *Helichrysum italicum*
ARTEMIS INTERNATIONAL	**Purple Corn** *Zea mays*
DMH ingredients inc	**Baobab** *Adansonia digitata*
	Rooibos *Aspalathus linearis*
afrigetics BOTANICALS	**Bulbine** *Bulbine natalensis*
BRASSICA	**Broccoli** *Brassica oleracea* Broccoli Group
indena®	**Indian Frankincense** *Boswellia serrata*
DownUnder enterprises	**Tea Tree** *Melaleuca alternifolia*
utzy naturals	**Black Chokeberry** *Aronia melanocarpa*
	Elderberry *Sambucus nigra*
	Stinging Nettle *Urtica dioica*
AFS APPLIED FOOD SCIENCES, INC.	**Kava** *Piper methysticum*
AMAZING HERBS	**Black Cumin** *Nigella sativa*
FOUR ELEMENTS	**Lemon Balm** *Melissa officinalis*
Teawolf Natural Extract Solutions	**Guayusa** *Ilex guayusa*
biotropics MALAYSIA	**Tongkat Ali** *Eurycoma longifolia*
Gaia Trading Company, Inc.	**Hops** *Humulus lupulus*
THE ACTIVES FACTORY	**Birch** *Betula* spp.

Become an adopter today!

Visit us at **www.herbalgram.org/adopt**

Adopt-an-Herb is an exciting and mutually beneficial way to support ABC!

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

Arnica *Arnica montana*
Photo ©2017 Steven Foster

Herbal Adopters

Aromatics Incorporated	**Peppermint** *Mentha x piperita*
Herbalife	**Aloe vera** *Aloe vera*
la-n USA	**Monk Fruit** *Siraitia grosvenorii*
travel medic travelmedic.net	**Kratom** *Mitragyna speciosa*
Naturopathica Holistic Health	**Arnica** *Arnica montana*
Future Ceuticals	**Coffee Fruit** *Coffea* spp.
KSM-66®	**Ashwagandha** *Withania somnifera*
Indfrag®	**Garcinia** *Garcinia cambogia*
Diana Performance from nature Food	**Acerola** *Malpighia* spp.
Schwabe North America / Nature's Way®	**Ginkgo** *Ginkgo biloba*
Natac Science to Market	**Olive** *Olea europaea*
Natac Science to Market	**Grape** *Vitis vinifera*
Pharmatoka	**Cranberry** *Vaccinium macrocarpon*
Ecoso Dynamics	**Devil's Claw** *Harpagophytum* spp.
EuroPharma	**Turmeric** *Curcuma longa*
Contains Zembrin	**Sceletium** *Sceletium tortuosum*
Mars symbioscience	**Cocoa Flavanols** *Theobroma cacao*
RFI From Field To Formula	**Hibiscus** *Hibiscus sabdariffa*
SFI™	**Bacopa** *Bacopa monnieri*
Vit-Best Nutrition	**Cinnamon** *Cinnamomum verum*

ABC Recognizes Herb Adoptions by FutureCeuticals and Naturopathica

In late 2016, the American Botanical Council (ABC) announced the adoption of coffee fruit (*Coffea* spp., Rubiaceae) by VDF FutureCeuticals, Inc., and recognized the past adoption of arnica (*Arnica montana*, Asteraceae) by Naturopathica. Their adoptions benefit ABC's Adopt-an-Herb program, which supports ABC's HerbMedPro database, a comprehensive, interactive online tool that provides access to important scientific and clinical research data on the uses and health effects of more than 250 herbs.

FutureCeuticals Adopts Coffee Fruit

Distinct from the coffee bean, coffee fruit contains higher levels of phenolic acids and antioxidative compounds than other so-called "super fruits." Through FutureCeuticals' generous support, ABC ensures that new, up-to-date scientific publications related to coffee fruit are entered into the extensive HerbMedPro database in a timely manner.

"For many years, ABC has been a major thought leader and contributor to a higher road within the natural foods and dietary supplement industries," said John Hunter, FutureCeuticals' executive vice president. "We have long respected and admired Mark Blumenthal, whose groundbreaking crusades for better standards to test botanical identity and improved manufacturing practices are well known to us all. His campaigns against botanical adulteration have led to important industry changes. Naturally, when we were invited to participate in the Adopt-an-Herb program by sponsoring coffee fruit, we were very pleased."

Blumenthal, ABC's founder and executive director, said: "ABC is deeply grateful to the folks at FutureCeuticals for adopting coffee fruit on ABC's HerbMedPro database. This adoption will allow ABC compilers and database editors to stay abreast with any and all recent scientific publications on coffee fruit."

About Coffee Fruit

Coffee fruit, which is the fruit of the coffee tree, provides low levels of caffeine, high levels of phenolic compounds with antioxidant activity, and riboflavin. Coffee fruit refers to the whole cherry, which includes the bean. Research on coffee fruit currently explores its antioxidant properties, effects on brain function, and effects on athletic performance. Preliminary clinical studies have shown that an extract of coffee fruit stimulates the production of Brain-Derived Neurotrophic Factor (BDNF), a neuroprotein known to be central to brain health. Additionally, a whole coffee fruit powder was shown to increase levels of Nrf2, a transcription factor known to regulate expression of antioxidant proteins that promote healthier aging and protect against oxidative damage.

About FutureCeuticals

Built upon deep agricultural roots, FutureCeuticals supplies and manufactures ingredients for the dietary supplement, functional foods, and cosmetics industries. The company is committed to creating a simplified supply chain, which includes being a leader in research and development, delivering the highest-quality raw materials, and providing material transparency via customer-centric quality programs. FutureCeuticals owns a number of brands including its proprietary Coffeeberry brand line of powders, extracts, and concentrates made from coffee fruit. More information is available at www.futureceuticals.com.

Naturopathica's Adoption of Arnica

Naturopathica, a wellness company with healing arts centers, skin and body care products, herbal remedies, and holistic health treatments, was the first company to support the Adopt-an-Herb program upon its launch in 2009. The company sells numerous botanical-based products, includ-

Coffee *Coffea arabica*
Photo ©2017 Steven Foster

ing three that contain arnica flower extract: Arnica Muscle & Joint Gel, Alpine Arnica Bath & Body Oil, and Mighty Mint Rescue Cream. Through Naturopathica's ongoing support, ABC ensures that new, up-to-date scientific publications related to arnica are entered into HerbMedPro.

"ABC is deeply grateful to Naturopathica for its support of ABC's nonprofit educational mission by adopting arnica in ABC's robust HerbMedPro database," said ABC Founder and Executive Director Mark Blumenthal. "Naturopathica's adoption allows ABC to ensure that the arnica record is up-to-date with the latest scientific and clinical research papers, just shortly after they are published, so researchers and others can access the totality of arnica-based research in a unique, time-saving organized format in HerbMedPro."

About Arnica

Arnica montana, also known as European arnica, is a member of the daisy family (Asteraceae) and is native to Europe. Historically, arnica preparations have been used externally for their anti-inflammatory, anti-rheumatic, skin-conditioning, and muscle pain-reducing properties. Although there are some traditional internal uses for arnica, preparations of the herb are almost exclusively used externally, with the exception of certain highly diluted homeopathic products.

The species contains a variety of phytochemicals, including alkaloids, flavonoids, terpenoids, coumarins, and carotenoids. Modern human clinical trials have focused largely on the herb's anti-inflammatory effects, and recent studies support the ability of topical arnica preparations to reduce bruising and relieve the severity and duration of osteoarthritis symptoms.

About Naturopathica

Naturopathica is "21st Century Wellness." The company empowers personal transformation with its healing arts centers, remedies, and rituals. Founder and product architect Barbara Close, a lifelong practitioner of natural health, creates skin care and body care products, herbal remedies, and holistic health treatments that support individuals on their path to wellbeing. Close has a master's degree in therapeutic herbalism from the Maryland University of Integrative Health and holds credentials in esthetics, advanced massage, and aromatherapy. Today, Naturopathica can be discovered through its Healing Art Centers & Spas in East Hampton and New York City, New York, its spa partners, and online at www.naturopathica.com.

ADOPT-AN-HERB
HerbMedPro™ PROGRAM

ABC's Adopt-an-Herb Program and HerbMedPro

FutureCeuticals and Naturopathica are two of the 40 companies that have supported ABC's educational efforts to collect, organize, summarize, and disseminate reliable, traditional, science-based, and clinical information 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, 45 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 result is an unparalleled resource not only for researchers, health professionals, industry, students, and consumers, but for all members of the herbal and dietary supplements community.

HerbMedPro is available to ABC members at the Academic level and higher. Twenty herb records are available for free to the public on HerbMedPro's "sister" site, HerbMed. 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

American Botanical Council: 2016 Year in Review

In 2016, the American Botanical Council (ABC) continued to advance its mission to educate and inform the public about a diverse range of topics related to medicinal plants and other beneficial botanicals. ABC is a recognized leader in the field of responsible, science-based herbal medicine education, and the nonprofit's efforts in 2016 — including the creation of a new series of Botanical Adulterants Bulletins — impacted community members both locally and internationally.

ABC reaches individuals in more than 80 countries using an array of educational services and platforms. These include numerous unique publications, an information-rich website, online databases, social media, lectures, consulting and research services, media education, an online bookstore, herbal demonstration gardens, educational events, and an internship program for students primarily from local universities. ABC's activities serve consumers, health care practitioners, academic researchers, educators, professionals from all segments of the natural products and health industries and extended communities, government employees, the media, and more.

Awards and Recognitions

In December, as part of the magazine's annual Best of the Industry awards, *Nutritional Outlook* recognized the ABC-American Herbal Pharmacopoeia (AHP)-National Center for Natural Products Research (NCNPR) Botanical Adulterants Program as an industry leader. *Nutritional Outlook* Editor-in-Chief Jennifer Grebow referred to the program as a "champion" of botanical adulteration awareness and education, and noted that its "positive effects are being felt not only within the industry but also where it matters most — consumer health and safety."[1]

Publication Projects and Milestones

Signifying "a new phase for the Botanical Adulterants Program,"[2] a new series of Botanical Adulterants Bulletins was announced in May 2016. The bulletins, which are designed to address ongoing issues related to botanical identity and adulteration, provide timely updates for quality control personnel, lab technicians, and other stakeholders in the herbal medicine, botanical ingredient, and dietary supplement industries. The program published bulletins for six herbs in 2016 — grape (*Vitis vinifera*, Vitaceae) seed extract, bilberry (*Vaccinium myrtillus*, Ericaceae) fruit extract, skullcap (*Scutellaria lateriflora*, Lamiaceae) herb, goldenseal (*Hydrastis canadensis*, Ranunculaceae) root and rhizome, black cohosh (*Actaea racemosa*, Ranunculaceae), and arnica (*Arnica montana*, Asteraceae). (At the time of this writing in early 2017, two additional bulletins have been published: St. John's wort [*Hypericum perforatum,* Hypericaceae] herb and extract, and saw palmetto [*Serenoa repens*, Arecaceae] fruit extract.)

In March, ABC launched another resource that provides continual updates for the herbal medicine community: the Herbal MediaWatch news feed. Available to the public for free on ABC's website, Herbal MediaWatch is a compilation of news articles, blog posts, and press releases on a range of herbal medicine- and functional food-related topics organized by category. Links to Herbal MediaWatch updates are also posted on ABC's Facebook and Twitter accounts.

For the first time, every issue of *HerbalGram* — dating back to issue 1 from 1983 — was made available online in at least one digital format to all ABC members. Previously, only issues 85 onward were available as PDF files. Now, all issues, including issues 1 through 21, which had never been available online in any format, are available as PDF files.

New ABC Staff Members

Anna Moreno, who served as the temporary executive assistant to Mark Blumenthal beginning in November 2015, was welcomed as part of ABC's permanent staff in March 2016. Moreno's previous work experience as an executive assistant, call center recruiter, and marketing promoter has helped her adapt quickly to her new role at ABC.

In April, Caroline Caswell began working as ABC's education assistant. In this role, Caswell works closely with Education Coordinator Jenny Perez, Special Projects Director Gayle Engels, and Head Gardener Toby Bernal. Caswell has a background as an herbalist, activist, and artist.

Tanya Garduño joined ABC in December 2016 as the new communications and marketing coordinator. Garduño has more than 10 years of nonprofit experience that has focused on communications, web design, and data management and analysis. With this background and expertise, she will play an integral role in helping ABC improve its online presence.

New Adopt-an-Herb Program Participants

In 2016, the 46th herb was adopted on ABC's HerbMedPro database through the ABC Adopt-an-Herb Program. The support of adopters helps ABC keep the records of adopted herbs up-to-date in its HerbMedPro database. The result is increased public awareness and access to reliable, science-based information on these and other herbs.

Through press releases, ABC recognized the following adoptions in 2016: sceletium (*Sceletium tortuosum*, Aizoaceae) by HG&H Pharmaceuticals; broccoli (*Brassica oleracea,* Brassicaceae) by Brassica Protection Products; cranberry (*Vaccinium macrocarpon*, Ericaceae) by Pharmatoka; black cohosh, hawthorn (*Crataegus* spp., Rosaceae), umckaloabo (*Pelargonium sidoides*, Geraniaceae), lavender (*Lavandula angustifolia*, Lamiaceae), and ginkgo (*Ginkgo biloba*,

Ginkgoaceae) by Nature's Way; kava (*Piper methysticum*, Piperaceae) by Applied Food Sciences; devil's claw (*Harpagophytum* spp., Pedaliaceae) by EcoSo Dynamics; coffee fruit (*Coffea* spp., Rubiaceae) by FutureCeuticals; and arnica by Naturopathica.

Other Notable Accomplishments

ABC also accomplished the following in 2016:

- ABC published its annual US Herb Market Report, which showed a 7.5% increase in total herbal supplement retail sales in 2015.
- ABC published its 6,600th HerbClip. HerbClips are insightful summaries and critiques of clinical studies and related botanical science publications.
- ABC submitted public comments on the US Drug Enforcement Administration's proposed scheduling of two alkaloids found in kratom (*Mitragyna speciosa*, Rubiaceae), and on the US Food and Drug Administration's new dietary ingredient draft guidance document.
- ABC published four issues of *HerbalGram,* 12 issues of HerbalEGram, 51 issues of Herbal News & Events, 360 HerbClips, six Botanical Adulterants Bulletins, and four Botanical Adulterants Monitor newsletters.
- ABC issued 29 press releases and fielded approximately 40 media requests. As a reliable third-party educational resource, ABC helps the media develop a more rational understanding and/or interpretation of scientific, regulatory, and market data. This year's interviews were featured in several major publications, including *The Wall Street Journal*, *The New York Times*, *New York Magazine*, and *National Geographic*, among others.
- ABC Chief Science Officer Stefan Gafner, PhD, co-authored two peer-reviewed scientific articles in the respected journal *Planta Medica*, and he was named one of the journal's top five peer reviewers for 2014 and 2015.
- The ABC-AHP-NCNPR Botanical Adulterants Program received endorsements from the National Animal Supplement Council, the Center for Natural Products Technologies at the University of Illinois at Chicago College of Pharmacy, and the Biodiversity and Medicines research cluster at the University College London School of Pharmacy. They join more than 180 other organizations and companies that have supported this program, which is designed to help improve the integrity of the global herb supply network.
- ABC trained 13 pharmacy and dietetic interns from sixth-year pharmacy school and graduate dietetic programs. Many of these interns were introduced for the first time to the science behind botanicals, herbal medicine, and various fruits, vegetables, culinary herbs, and spices for potential inclusion in their future practices.
- ABC hosted more than 500 visitors at its historic 2.5-acre headquarters throughout the year. These visitors included children, seniors, college students (including medical and nursing students), garden clubs, herbalists, health care providers, and other interested members of the local community. There was also a strong turnout at ABC's annual HerbDay celebration in May. HG

—ABC Staff

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American Botanical Council Welcomes 12 New Advisory Board Members

The American Botanical Council (ABC) welcomed 12 new members to its Advisory Board in 2016. These highly regarded professionals bring expertise in a wide variety of medicinal plant-related fields, including pharmacognosy, analytical testing, nutrition and aging, herbal product development, Chinese medicine, psychiatry, functional foods, and safety and risk assessments.

ABC Advisory Board members generously volunteer to review articles that appear in *HerbalGram*, HerbalEGram, HerbClip, and other peer-reviewed ABC publications. Additionally, ABC management and *HerbalGram* editors seek feedback and advice from Advisory Board members on research questions, article ideas, ABC policies, and book reviews, among many other topics.

Of the 12 new members, about half are based outside of the United States — in Australia, Canada, Iran, and Hong Kong — which broadens the international scope of the Advisory Board and helps ABC expand its educational impact. They join ABC's 126 current Advisory Board members, which includes 32 international experts.

"ABC is deeply pleased to welcome these expert scientists to our Advisory Board," said Mark Blumenthal, founder and executive director of ABC. "They will help enable and empower ABC's broad nonprofit educational mission, as well as provide added expertise and scientific accuracy to ABC's publications and programs."

ABC Chief Science Officer Stefan Gafner, PhD, added: "I am very happy to see the 12 new additions to our Advisory Board. The facets of research into medicinal herbs are so numerous that the expertise of our Advisory Board members is essential to competently fulfill ABC's educational mission, and to ensure the continuation of our authoritative coverage of such topics as traditional and evidence-based use, clinical trials, regulations, and quality control of herbal products."

ABC welcomes the following new Advisory Board members:

Hamid-Reza Adhami, PhD, PharmD, is an assistant professor in the department of pharmacognosy at Tehran University of Medical Sciences in Tehran, Iran, where he teaches courses on pharmacognosy, medicinal plants, and complementary and alternative medicine. His research interests include the isolation, characterization, and purification of biologically active secondary metabolites from natural sources. Adhami received his doctorate in pharmacognosy from the University of Vienna in 2012. He was a visiting researcher at the Brunel Institute for Bioengineering in London and completed his postdoctoral fellowship at the department of pharmaceutical sciences at Tshwane University of Technology in South Africa. He previously served as the secretary of the Division of Complementary and Alternative Medicine of the National Research Center for Medical Sciences of Iran and as the executive manager of the Pharmaceutical Incubator of Tehran University of Medical Sciences. In 2007, he co-authored the Farsi translation of the World Health Organization's (WHO's) Traditional Medicine Strategy, and has published multiple papers in both English and Farsi.

Lori L. Bestervelt, PhD, currently holds dual positions with NSF International as executive vice president and chief technical officer. In these roles, she directs NSF's global network of engineering, chemistry, and microbiology laboratories and toxicology services, and leads cross-functional collaborative efforts across all departments and divisions. Additionally, she helped lead the development of the only American National Standard for dietary supplements, as well as the corollary programs through which NSF tests and certifies dietary supplements to this standard. She has more than 25 years of experience in the fields of nutritional biochemistry, metabolism, and toxicology, addressing the safety of hundreds of materials used in dietary supplements, pharmaceuticals, and consumer products. She has developed risk assessments for the US Environmental Protection Agency and Health Canada, and has worked with the WHO on food and water safety issues. Before joining NSF, she worked as a scientist at Pfizer.

Jeffrey B. Blumberg, PhD, FASN, FACN, CNS-S, is a professor in the Friedman School of Nutrition Science and Policy in Boston, Massachusetts, and also serves as the senior scientist of the Antioxidants Research Laboratory at the Jean Mayer US Department of Agriculture (USDA) Human Nutrition Research Center on Aging at Tufts University in Boston. His research focuses on the biochemical basis for the role of antioxidant nutrients in promoting health and preventing disease during the aging process via changes in status of oxidative stress, glucoregulation, and inflammation. He has published more than 350 peer-reviewed scientific articles and serves on the editorial boards of several scientific journals. In 2015, Blumberg was included on the Thom-

son Reuters list of the World's Most Influential Scientific Minds. Blumberg also has served as a member of the Workshop on Health Promotion and Aging in the Office of the US Surgeon General, the Sports Medicine Committee of the US Olympic Committee, the Consultation on Preparation and Use of Food-Based Dietary Guidelines for the WHO, and other scientific and nutritional committees.

Heather Boon, BScPhm, PhD, is the dean of the Leslie Dan Faculty of Pharmacy at the University of Toronto in Ontario, Canada, where she lectures on natural health products and complementary medicine. She is the founding chair of the Canadian Interdisciplinary Network for Complementary and Alternative Medicine Research and is the past president of the International Society of Complementary Medicine Research. She served as the chair of Health Canada's Expert Advisory Committee for Natural Health Products from 2006-2009. Her primary research interests are the safety and efficacy of natural health products as well as traditional/complementary/alternative medicine regulation and policy issues. She is the author of a textbook on natural health products and more than 150 academic publications. Boon currently is an advisor for the Centre for Critical Qualitative Health Research at the University of Toronto.

Robert G. Chapman, PhD, is the principal research officer of the National Research Council Canada's Aquatic and Crop Resource Development Portfolio, where he is responsible for leading strategic projects that aim to develop new functional ingredients, including nutritional oils and plant-based proteins. He has 10 years of experience working with companies in the private sector to help improve the overall quality attributes of their functional ingredients through application of modern analytical methodologies. Chapman also helps educate those within the natural products industry through presentations that emphasize the importance of quality control in manufacturing and the tools available for choosing the best functional ingredients for finished products. He is also an adjunct professor in the department of chemistry at the University of Prince Edward Island in Charlottetown, PEI, Canada.

Holly E. Johnson, PhD, laboratory director at Alkemist Labs, joined the company in 2014, leading project teams in analytical testing of natural products and botanical ingredients as well as performing specialized research. Johnson obtained her doctorate in pharmacognosy at the University of Illinois at Chicago College of Pharmacy under the supervision of renowned pharmacognosist Norman R. Farnsworth, PhD. She was awarded a National Institutes of Health (NIH) National Research Service Award Fellowship and worked in the NIH Center for Botanical Dietary Supplements for Women's Health. Johnson received bachelor's degrees in environmental biology and botany from the department of biological sciences at Humboldt State University in Arcata, California. In her ethnobotanical research, Johnson has led numerous field expeditions collecting plants and working with indigenous healers, and she is currently a research associate with the federally chartered National Tropical Botanical Garden. She also worked for Waters Corporation conducting technical courses and consulting on chemistry applications and regulatory compliance for pharmaceutical and supplement companies. Johnson serves on advisory boards for the American Herbal Pharmacopoeia and on expert review panels and stakeholder panels for dietary supplements at AOAC International. She is also on the editorial board of the *Journal of AOAC International*. Johnson has 19 years of experience in natural products chemistry with botanicals and spent many years conducting research on medicinal plants and teaching courses at the University of Hawaii.

John McPartland, DO, is an osteopathic physician who has worked at Vermont Alternative Medicine, Inc., a private practice in Middlebury, Vermont, since 1993. McPartland received his MS in plant pathology from the University of Illinois and his DO from the Chicago College of Osteopathic Medicine. He completed a residency in family practice at the University of Pittsburgh and a fellowship in biomechanics at Michigan State University. He first learned about medicinal plants at Boy Scout camp under the tutelage of Euell Gibbons. McPartland has authored more than 150 publications in peer-reviewed journals, including work on *Phyllanthus amarus* (Euphorbiaceae), milk thistle (*Silybum marianum*, Asteraceae), saw palmetto (*Serenoa repens*, Arecaceae), American ginseng (*Panax quinquefolius*, Araliaceae), and psychotropic mushrooms. He began cannabinoid research in 1981 and was the last person issued a new DEA Schedule I license to cultivate *Cannabis* spp. (Cannabaceae). Since 1997, he has worked as a clinical assistant professor in the department of family medicine at the University of Vermont. In 1999, McPartland began a consultancy with GW Pharmaceuticals exploring cannabis and the endocannabinoid system. His *HerbalGram* subscription goes back to 1988.

James Neal-Kababick is the founder and director of Flora Research Laboratories, LLC, which specializes in the research and analysis of botanicals, dietary supplements, and related compounds. He is also adjunct faculty at

Bastyr University in Kenmore, Washington, where he teaches botanical drug identification by microscopy and thin-layer chromatography. In addition to his work at the private research lab and university, he serves on multiple expert committees for AOAC International, the United States Pharmacopeia (USP), the NIH, the American Herbal Products Association, and others. Currently, his work focuses on modern analytical technologies in the investigation of dietary supplements and other agricultural products. His collaborations include the development of databases and spectral libraries for rapid identification of botanicals, compounds, and clandestine drugs, as well as presenting lecture series and teaching hands-on training courses in the phytoforensic sciences.

Jerome Sarris, PhD, is a professor of integrative mental health and the deputy director of the National Institute of Complementary Medicine at Western Sydney University. Previously, he was a senior research fellow in the department of psychiatry at the University of Melbourne. He holds a master's degree in herbal medicine, and his doctorate in the field of psychiatry involved the study of plant medicines for depression and anxiety. His research interests include anxiety and mood disorders, nutraceutical psychopharmacology, integrative medicine research, and psychotropic medicinal plants (including significant work on kava [*Piper methysticum*, Piperaceae]). Sarris was a co-founding vice chair of the International Network of Integrative Mental Health, and he is an executive board member of the International Society for Nutritional Psychiatry Research. He has published more than 100 peer-reviewed scientific articles in various high-impact journals, including *The American Journal of Psychiatry* and *Lancet Psychiatry*, and is currently conducting several clinical trials on the mental health applications of plant medicines.

Natascha Techen, PhD, is a senior research scientist at the National Center for Natural Products Research at the University of Mississippi (Ole Miss) in Oxford, Mississippi. Prior to her current position, Techen worked at Ole Miss as a postdoctoral research biologist from 2002-2010 and a research scientist from 2010-2016. In 2002, Techen received a doctorate in plant molecular biology from the University of Hamburg in Germany, where she also obtained her bachelor's and master's degrees, both in molecular biology. She has given numerous oral presentations and authored more than 20 scientific journal articles, many of which have focused on DNA barcoding analyses of botanical dietary supplements and other plant-based materials. Techen has been a member of the American Society of Pharmacognosy since 2005, and has served as a peer reviewer for *Methods in Molecular Biology*, the *Journal of Ethnopharmacology*, and *Planta Medica*, among many other journals.

Michael Tims, PhD, has served as the academic director of herbal programs at the Maryland University of Integrative Health since 2012. In 1999, he founded Radix Medicina, where he currently works as an herbal product development consultant. Tims received his doctorate in the chemical ecology of medicinal plants from the University of Maryland, College Park. He has worked as a clinical herbalist, a managing partner of Cash Grocer Natural Foods in Alexandria, Virginia, and an academic researcher. His current research interests include rhizosphere chemical ecology, botanical pharmacognosy, and rational botanical extraction method design, among others. Tims is a member of the International Society of Chemical Ecology, the National Association of Science Writers, and other professional organizations. He has written numerous scientific journal articles and Reports of Analysis for the National Institutes of Standards and Technology. He has also given oral presentations on a wide range of topics. Tims is the author of *The Chemical Ecology of Goldenseal* (VDM Verlag, 2008), the Botanical Adulterants Bulletin on goldenseal for the ABC-AHP-NCNPR Botanical Adulterants Program, and a book of poems, titled *The Acoustic Properties of Ancient People* (in press, Finishing Line Press, 2017).

Zhongzhen Zhao, PhD, MH, is the associate dean and chair professor of the Teaching and Research Division at Hong Kong Baptist University (HKBU), where he has worked since 1999. He was a founding member of HKBU's School of Chinese Medicine and played a key role in establishing the HKBU Bank of China (HK) Chinese Medicines Centre, which houses more than 10,000 Chinese medicinal plant specimens. Zhao received his doctorate from Tokyo University of Pharmacy and Life Sciences and his bachelor's and master's degrees from Beijing University of Traditional Chinese Medicine. His research interests include pharmacognosy, herbal medicine quality assurance, the history of Chinese medicine, and the authentication of Chinese materia medica, among others. Since 2003, Zhao has served on the scientific and international advisory boards of the Hong Kong Chinese Materia Medica Standards Office, and he is a member of the USP Dietary Supplements-Botanicals Expert Committee. He has also participated in various herbal medicine-related committees of the NIH, the WHO, and other organizations. He has given numerous oral presentations and lectures, and is the lead author of more than 80 peer-reviewed scientific journal articles. HG

—ABC Staff

ABC Requests FDA to Continue to Revise the New Dietary Ingredient Draft Guidance

ABC says NDI draft guidance exceeds scope of current law and intent of Congress

On December 12, 2016, the nonprofit American Botanical Council (ABC) filed comments in response to the US Food and Drug Administration's (FDA's) revised draft guidance for industry, titled "Dietary Supplements: New Dietary Ingredient Notifications and Related Issues."[1]

ABC stated in its comments to the FDA that the draft guidance exceeds the original intent of Congress behind the Dietary Supplement Health and Education Act of 1994 (DSHEA)[2] — the hallmark piece of bipartisan legislation that created a regulatory framework specific to dietary supplements — and requests the FDA to revise the 2016 draft guidance to more closely align with the intent and explicit text of DSHEA.

At issue is the FDA's development of a guidance document that is intended to provide more exact instructions to the industry on how to bring a "new dietary ingredient"[3] (NDI) to market.

DSHEA outlines two types of dietary ingredients that are allowed in dietary supplement products: "Grandfathered" ingredients or dietary ingredients that were marketed pre-DSHEA (before October 15, 1994), and NDIs that were *not* marketed pre-DSHEA. Regardless of whether a dietary ingredient is grandfathered or an NDI, a manufacturer must comply with each labeling and safety provision of DSHEA, including the adulteration[4] section and current Good Manufacturing Practices (cGMPs).[5]

However, if the ingredient is an NDI, a manufacturer or distributor of the NDI or dietary supplement product that contains the NDI must notify the FDA 75 days *before* going to market with the basis for concluding that the NDI, when used under recommended conditions, will reasonably be expected to be safe.[6] The FDA and various members of the herb and dietary supplement industry have a difference in opinion on what data and information are needed to satisfy the standard of "reasonably be expected to be safe."

The amount of time it took the FDA to issue the revised draft gudiance is an indication of the complexity of the matter. In 1997, three years after DSHEA was passed, the FDA issued a Final Rule[7] (regulations) on the NDI provision within DSHEA that provided the procedure for NDI notifications. Then, in 2004 — 10 years after DSHEA was passed — the FDA held a meeting and solicited comments from the public and industry "concerning the content and format requirements for NDI notifications." The FDA wanted the input to clarify the type, quantity, and quality of information that should be included in NDI notifications to the FDA.[8] In 2011, the FDA issued

ABC wishes to see rational regulations and guidance from the government that protects consumers from inauthentic and/or unsafe products and also allows members of industry to be able to produce supplements that meet or exceed required federal regulations for quality and safety.

a draft NDI guidance — 17 years after DSHEA — which received a large volume of comments from the public. The FDA never finalized the 2011 guidance document. Then, in August of 2016, the FDA issued a revised draft NDI guidance document — 22 years after DSHEA — and that version is the subject of ABC's comments.

One of ABC's several primary concerns with the 2016 draft guidance is the FDA's focus on — and request for significant information on — the dietary supplement product itself. ABC set forth that the language in the NDI provision in DSHEA speaks to the *dietary ingredient* versus the finished dietary supplement product. ABC also references historic FDA actions that support the position that an NDI notification concerns the ingredient.

ABC also expressed its concerns that the FDA's language in the 2016 draft guidance suggests that almost *any* change in the manufacturing process or solvent used to make an extract might require an NDI notification due to possible chemical alteration of the ingredient. ABC provided examples in which such chemical alteration may justifiably warrant an NDI notification and where it can be relatively insignificant and should not require a notification.

"As an independent nonprofit research and education organization, and as the founding and lead organization in an international consortium of medicinal plant research and analytical experts focusing on herb identity and quality control, ABC supports the proposition that all botanical ingredients used in dietary supplements should be authentic, properly tested for their identity, and safe for their intended use," said Mark Blumenthal, ABC founder and executive director.

Blumenthal added: "ABC wishes to see rational regulations and guidance from the government that protects consumers from inauthentic and/or unsafe products and also allows members of industry to be able to produce supplements that meet or exceed required federal regulations for quality and safety. However, some provisions proposed by the FDA go well beyond what Congress intended when it conceived of NDIs and what the law actually requires, and ABC is concerned that the FDA's proposed guidance will not result in any meaningful consumer benefit."

Even though guidance documents are not binding for the FDA or the industry, ABC believes that an FDA guidance document sets a precedent and important guardrails to industry and regulators. Therefore, ABC recommended that the FDA revise the 2016 draft guidance to align with the intent of Congress and the explicit text of Section 8 of DSHEA. ABC also encouraged the FDA to continue to prioritize enforcement measures on adulterated raw materials sold as dietary ingredients, adulterated and mislabeled products, and violations of government-mandated cGMPs, since these areas have a greater likelihood of positive impact on product quality and public health. HG

—Tami Wahl

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2. Dietary Supplement Health and Education Act of 1994 (DSHEA), Pub. L. 103–417, 108 Stat. 4325.
3. Food, Drug, and Cosmetic Act (FDCA) §413 (21 USC §350b).
4. FDCA §413 (21 USC §342(f)), Adulterated food.
5. 21 CFR 111, Current Good Manufacturing Practice in Manufacturing, Packaging, Labeling, or Holding Operations for Dietary Supplements.
6. 21 USC §350b(a)(2), New dietary ingredients.
7. 21 CFR 190.6, New Dietary Ingredient Notification, Requirement for premarket notification (62 Federal Register 49886, Sept. 23, 1997).
8. Food and Drug Administration, Dietary Supplements; Premarket Notification for New Dietary Ingredient Notifications; Public Meeting, 69 *Federal Register* 61680 (October 20, 2004).

ABC Requests DEA Not to Proceed with Restrictive Scheduling of Kratom

Potential medical/therapeutic uses of kratom warrant further scientific research

On December 1, 2016, the nonprofit American Botanical Council (ABC) filed comments in response to the US Drug Enforcement Administration's (DEA's) request for comments on the proposed listing of two compounds found in the Southeast Asian herb kratom (*Mitragyna speciosa*, Rubiaceae) in Schedule I of the Controlled Substances Act (CSA).

Schedule 1 substances are "those that have a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision."

In its comments, ABC stated that emerging scientific evidence supports potential medical uses of the kratom alkaloids mitragynine and 7-hydroxymitragynine, and that placing these substances in Schedule I of the CSA may impede current and future medical research efforts. ABC also acknowledged the actions that the US Food and Drug Administration (FDA) — the principal federal agency with enforcement authority over food, dietary supplement, and drug products — has initiated to remove certain kratom-containing products from the marketplace.[1] ABC emphasized that these FDA enforcement efforts should continue to ensure that only kratom products that comply with FDA regulations are available in the market.

Due to the almost 15,000 comments received from the public, Congressional members, and the scientific community, the DEA withdrew its original August 31, 2016, notice of intent to temporarily schedule the alkaloids, and instead, opened a comment period through December 1, 2016. (Since the comment period has ended, the DEA may choose to proceed with a temporary and/or permanent scheduling of these substances. If the DEA determines a permanent scheduling is warranted, it will publish a notice of proposed rulemaking in the *Federal Register,* which will allow for an additional public comment period.) The DEA intended to use this time to consider the extensive comments already received, to solicit additional information from the public, and to request the FDA's expedited scientific and medical evaluation and scheduling recommendation for these substances.

ABC has reviewed the scientific literature related to kratom and, in *HerbalGram* issue 112, published an extensive peer-reviewed article on this plant and the various issues related to its use.[2] The article also served as the foundation of ABC's comments to the DEA.

ABC stated that there is a growing body of evidence that indicates that kratom and its constituents may have the potential to be safe and effective pain-relievers and recovery aids for opioid addiction or dependence. ABC also noted that further research is needed to fully discover kratom's medicinal value and its potential risks and safety considerations, such as addiction potential. However, ABC referenced medical research that suggests that kratom's addictive potential is significantly less than that of common opioids.

ABC also emphasized that by putting these substances in Schedule I, the medical research community will be subject

Kratom *Mitragyna speciosa*
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(iStockPhoto.com)

to additional hurdles — such as obtaining a license from the DEA (and likely a state registration), along with other security, inventory, and recordkeeping requirements[3] — that may impede and/or curtail current and future research efforts.

"ABC realizes that there are compelling scientific data to support kratom's potential therapeutic uses; there is also confusion about its safety profile," said Mark Blumenthal, founder and executive director of ABC. "Our comments to the DEA are intended to help ensure that appropriate scientific and medical research on this interesting plant and its biologically active constituents can continue with minimal regulatory hurdles."

To add further support to ABC's position that the DEA should not list these substances in Schedule I, ABC raised concerns regarding the data cited by the DEA to support the temporary scheduling. Specifically, ABC believes the safety profile of the plant is not wholly known, and that a more thorough investigation of the relationship between kratom and adverse event reports provided by the poison control call centers needs to be performed. For example, some of the data cited by the DEA include cases of kratom being used with various analgesic and/or sedative pharmaceutical drugs. Also, ABC noted that, in many cases, there was a lack of analytical testing of commercial kratom products to identify the possible presence of other substances that may have contributed to the adverse reactions.

ABC believes that the potential benefits of kratom warrant further scientific and medical investigation, and that putting kratom compounds in Schedule I would create excessive obstacles to research on a plant that could benefit a large number of people. HG

—Tami Wahl

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2. Yearsley C. Kratom: medicine or menace? *HerbalGram*. 2016;112:46-59.
3. 21 CFR §1301, Registration of Manufacturers, Distributors, and Dispensers of Controlled Substances.

Botanical Adulterants Program Named 'Best of Industry' for 2016 by *Nutritional Outlook*

***Nutritional Outlook*, one of the leading trade publications in the United States natural products industry, recognized the ABC-AHP-NCNPR Botanical Adulterants Program as an "Industry Leader" in its "Best of the Industry 2016" awards, lauding the program for its "industry-advancing contributions" against accidental and intentional adulteration of botanical products. *Nutritional Outlook* further praised the timeliness of the information the program provides, as well as its breadth and depth due to its multiple publications, including the Botanical Adulterants Monitor newsletter, the Botanical Adulterants Bulletins, and the Laboratory Guidance Documents.[1]**

The addition of peer-reviewed Botanical Adulterants Bulletins in 2016 received special mention. "These concise (but still information-packed) reviews of ingredient-specific botanical adulteration are not as in-depth as full-scale Botanical Adulteration Reports [published in *HerbalGram*], but are still jam-packed with crucial information," wrote Jennifer Grebow, editor-in-chief of *Nutritional Outlook*, in the announcement. Though the program is a coalition of nonprofit organizations and is not a member of the industry per se, it seeks to make information available about botanical adulteration and its detection to stakeholders, which include dietary supplement manufacturers, contract laboratories, and others along the botanical supply chain.

"All of us who work in the Botanical Adulterants Program are deeply grateful to our friends at *Nutritional Outlook* for deeming our efforts worthy of recognition," said Mark Blumenthal, founder and executive director of ABC and director of the Botanical Adulterants Program. "It is through such high-profile coverage in the herb, dietary supplement, and natural products industries that we will continue to be successful in our objectives of educating industry members about the presence of adulterated botanical materials and how to detect and avoid it. Our publications are used by many industry members when developing specifications for their botanical ingredients to help ensure high-quality products for consumers." HG

—ABC Staff

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1. Grebow J. *Nutritional Outlook*'s 2016 Best of the Industry, Industry Leader: Botanical Adulterants Program. December 7, 2016. *Nutritional Outlook*. Available at: www.nutritionaloutlook.com/herbs-botanicals/nutritional-outlooks-2016-best-industry-industry-leader-botanical-adulterants-program. Accessed January 4, 2017.

New Botanical Adulterants Bulletins Published on Saw Palmetto and St. John's Wort

In early 2017, the American Botanical Council (ABC)-American Herbal Pharmacopoeia (AHP)-National Center for Natural Products Research (NCNPR) Botanical Adulterants Program published new Botanical Adulterants Bulletins (BABs) on saw palmetto (*Serenoa repens*, Arecaceae) berry and berry extracts, and St. John's wort (*Hypericum perforatum*, Hypericaceae) extracts. The St. John's wort and saw palmetto bulletins are the seventh and eighth publications, respectively, in the Program's series of BABs.

The goal of the BABs 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, dietary supplement, cosmetic, conventional food, and other industries in which botanical ingredients are used to be informed on adulteration problems that are apparently widespread and/or may constitute safety problems. As with all publications of the program, the bulletins are freely accessible on the program's website to all ABC members and registered users of the ABC website.

Saw Palmetto Bulletin Describes Adulteration with Low-Cost Vegetable Oils

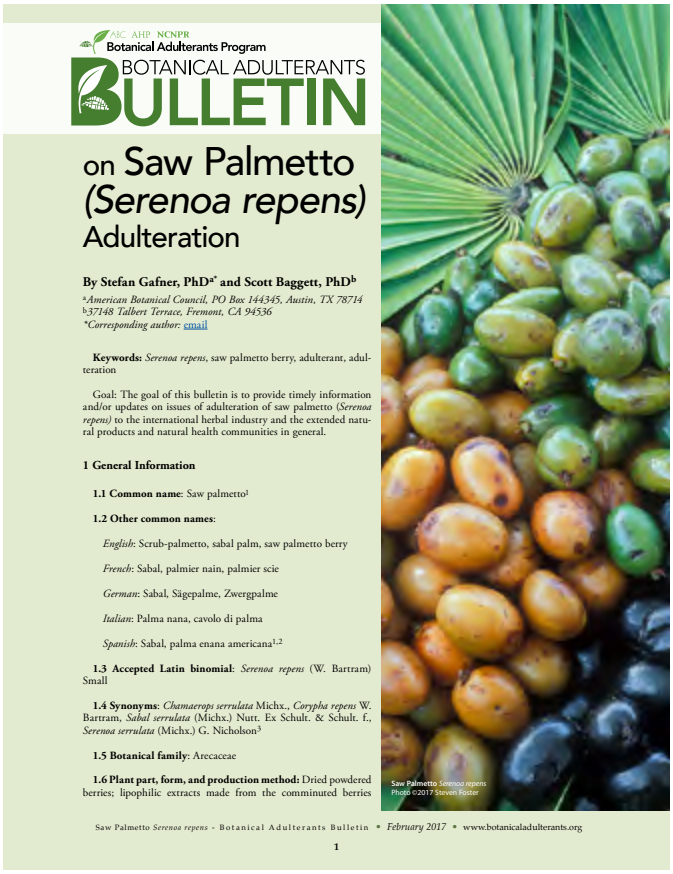
Saw palmetto extract is a popular ingredient in dietary supplements used for normalizing prostate function and relieving lower urinary tract symptoms (e.g., inability to void urine) related to benign prostatic hyperplasia. The 2016 *HerbalGram* Herb Market Report ranked saw palmetto products among the 20 top-selling herbal supplements for 2015 in both mainstream and natural retail outlets in the United States.

Reports of the addition of undeclared vegetable oils (e.g., palm [*Elaeis* spp., Arecaceae] oil, canola [*Brassica* spp., Brassicaceae] oil, or coconut [*Cocos nucifera*, Arecaceae] oil) to saw palmetto extracts for financial gain appeared in the early 2000s. Since these vegetable oils contain some of the same components as ripe saw palmetto berries, the detection of this type of adulteration is not always straightforward. Even more difficult is the determination of the exact amount of saw palmetto in a finished product, since vegetable oils sometimes are added as excipients (and appropriately declared on the label) as part of the semi-liquid formulation of the saw palmetto extract (e.g., in soft-gel capsules). Unscrupulous suppliers have taken advantage of these analytical challenges to pass off vegetable oils as saw palmetto extracts entirely and/or to dilute saw palmetto extracts with the lower-cost vegetable oils.

The saw palmetto bulletin was co-authored by Scott Baggett, PhD, an analytical methods consultant for the natural products industry, and Stefan Gafner, PhD, ABC chief science officer and Botanical Adulterants Program technical director. Besides information on production, supply sources, and market importance of saw palmetto and its extracts, the bulletin provides information about known adulterants and analytical approaches to detect adulterants. Ten expert peer reviewers provided input on the saw palmetto bulletin.

"The saw palmetto plant grows and produces fruit (called 'berries' in the trade) only in the southeastern United States, mainly Florida," said Mark Blumenthal, founder and executive director of ABC and founder and director of the Botanical Adulterants Program. "We have heard concerns for many years from ethical, responsible members of the industry about saw palmetto extracts being adulterated with low-cost vegetable oils. This creates unfair competition and reduces the potential health benefit to men who use saw palmetto to help manage urinary conditions."

Blumenthal continued: "There are high-quality saw palmetto extracts in the world market that are the subject of numerous published clinical trials that demonstrate their safety and potential benefits in prostate health. Consumers should be able to purchase these and other saw palmetto supplements with a sense that they contain appropriate amounts of true, authentic saw palmetto."



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BOTANICAL ADULTERANTS BULLETIN

on Saw Palmetto (*Serenoa repens*) Adulteration

By Stefan Gafner, PhD[a*] and Scott Baggett, PhD[b]

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Keywords: *Serenoa repens*, saw palmetto berry, adulterant, adulteration

Goal: The goal of this bulletin is to provide timely information and/or updates on issues of adulteration of saw palmetto (*Serenoa repens*) to the international herbal industry and the extended natural products and natural health communities in general.

1 General Information

1.1 Common name: Saw palmetto[1]

1.2 Other common names:

English: Scrub-palmetto, sabal palm, saw palmetto berry

French: Sabal, palmier nain, palmier scie

German: Sabal, Sägepalme, Zwergpalme

Italian: Palma nana, cavolo di palma

Spanish: Sabal, palma enana americana[1,2]

1.3 Accepted Latin binomial: *Serenoa repens* (W. Bartram) Small

1.4 Synonyms: *Chamaerops serrulata* Michx., *Corypha repens* W. Bartram, *Sabal serrulata* (Michx.) Nutt. Ex Schult. & Schult. f., *Serenoa serrulata* (Michx.) G. Nicholson[3]

1.5 Botanical family: Arecaceae

1.6 Plant part, form, and production method: Dried powdered berries; lipophilic extracts made from the comminuted berries

Saw Palmetto *Serenoa repens*
Photo ©2017 Steven Foster

Saw Palmetto *Serenoa repens* - Botanical Adulterants Bulletin • *February 2017* • www.botanicaladulterants.org

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The distinction between the various *Hypericum* species is challenging, and a good control over the supply chain is crucial. For laboratory analysts, more data on the morphological, phytochemical, and genetic differences among closely related species would be beneficial to help ensure the presence of authentic St. John's wort.

Gafner added: "The sale of adulterated extracts is known to reputable manufacturers of authentic saw palmetto extracts and to many responsible manufacturers of saw palmetto dietary supplements, but there is a lack of reliable data on the extent of the problem in the peer-reviewed scientific literature. Of particular concern are raw materials labeled as 'saw palmetto extract' that are imported from China, where saw palmetto is not known to grow. We hope that this bulletin will help raise awareness of this adulteration issue and ultimately increase the number of high-quality products in the market."

St. John's Wort Bulletin Details Adulteration with Food Dyes, Extracts from Other *Hypericum* Species

Extracts of St. John's wort are widely used for the symptomatic treatment of mild-to-moderate depression. According to data from the *Nutrition Business Journal*, sales of St. John's wort dietary supplement products in the United States alone reached $57 million in 2015.

The unintentional collection of closely related *Hypericum* species instead of authentic St. John's wort was described as early as the 1980s. The addition of food dyes to St. John's wort extracts with the aim to fool standard laboratory tests (spectrophotometric determination of total hypericins) in order to comply with the labeled contents has been documented only recently.

The new bulletin, written by Allison McCutcheon, PhD, an herbal research expert in British Columbia, Canada, provides information on the growing range, production, and market importance of St. John's wort and its extracts. It also lists the known adulterants, potential therapeutic and/or safety issues with known adulterants, and analytical approaches to detect adulterants. Sixteen expert peer reviewers provided input on the St. John's wort bulletin.

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BOTANICAL ADULTERANTS BULLETIN

on Adulteration of *Hypericum perforatum*

By Allison McCutcheon, PhD

Correspondence: email

Keywords: Adulterant, adulteration, St. John's wort, *Hypericum perforatum*, *Hypericum barbatum*, *Hypericum hirsutum*, *Hypericum montanum*, *Hypericum patulum*, *Hypericum tetrapterum*, food dyes, E123 Amaranth, E133 Brilliant Blue, E110 Sunset Yellow, E102 Tartrazine)

Goal: The goal of this bulletin is to provide timely information and/or updates on issues of adulteration of St. John's wort (*Hypericum perforatum*, Hypericaceae) to the international herbal industry and extended natural products community in general. It is intended to complement the previously published works with information on St. John's wort (SJW) adulteration, e.g., the American Herbal Pharmacopoeia (AHP) SJW monograph,[1] by presenting new data on the occurrence of adulteration, the market situation, and consequences for the consumer and the industry.

1 General Information

1.1 Common name: St. John's wort

1.2 Other common names:

English: Common St. John's wort, perforate St. John's wort, goatweed, Klamath weed, racecourse weed, tipton weed[2-4]
Chinese: Guan ye lian qiao (贯叶连翘),[3-5] (千層樓)[2]
Dutch: Sint-janskruid[2,3]
French: Millepertuis, herbe à mille trous; millepertuis perforé, herbe de la Saint Jean, toutsaine[2,3]
German: Johanniskraut, Johannisblut, Herrgottsblut, Tüpfelhartheu, Tüpfel-Johanniskraut[2,3]
Italian: Iperico, erba di San Giovanni, iperico perforato, perforata, pilatro[2,3]
Portuguese: Hipericão, milfurada[3]
Russian: Zveroboj obyknovenny,[4] zwieroboij[2,3]
Spanish: Corazoncillo, hierba de San Juan, hipericón[2,3]
South African: Johanneskruid[3,4]
Swedish: Äkta johannesört,[4] Johannesört[3]
1.3 Accepted Latin binomial: *Hypericum perforatum* L.[6,7]
1.4 Synonym: *H. vulgare* Lam.[3]
1.5 Botanical family: Hypericaceae

Hypericum perforatum - Botanical Adulterants Bulletin • *January 2017* • www.botanicaladulterants.org

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St. John's Wort *Hypericum perforatum*
Photo ©2017 Steven Foster

The new bulletin, written by Allison McCutcheon, PhD, an herbal research expert in British Columbia, Canada, provides information on the growing range, production, and market importance of St. John's wort and its extracts. It also lists the known adulterants, potential therapeutic and/or safety issues with known adulterants, and analytical approaches to detect adulterants. Sixteen expert peer reviewers provided input on the St. John's wort bulletin.

"Adulteration of St. John's wort extracts with chemical dyes is no accident," said Blumenthal. "Detection of these dyes by use of appropriate analytical methods in industry laboratories is an important step in preventing fraudulent and ineffective extracts from being sold to consumers. This is one of the key objectives of our Botanical Adulterants Program."

Gafner noted: "The sale of St. John's wort extracts that contain undeclared food dyes has been reported by a number of analysts from industry and contract analytical laboratories. This type of adulteration is quite easily detected with appropriate analytical methods."

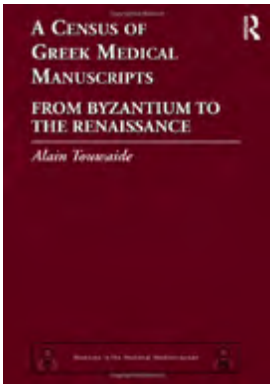
"The distinction between the various *Hypericum* species is challenging, and a good control over the supply chain is crucial," Gafner continued. "For laboratory analysts, more data on the morphological, phytochemical, and genetic differences among closely related species would be beneficial to help ensure the presence of authentic St. John's wort."

BABs are also available on the adulteration of arnica (*Arnica montana*, Asteraceae) flower, bilberry (*Vaccinium myrtillus*, Ericaceae) fruit extract, black cohosh (*Actaea racemosa*, Ranunculaceae) root and rhizome, goldenseal (*Hydrastis canadensis,* Ranunculaceae) root and rhizome, grape (*Vitis vinifera*, Vitaceae) seed extract, and skullcap (*Scutellaria lateriflora*, Lamiaceae) herb. HG

—ABC Staff

Census of Greek Medical Manuscripts Illuminates Centuries of Herbal Medicine Practice

In the late 19th and early 20th centuries, classical scholar Hermann Diels guided a team of philologists (scholars who study literary sources and records to establish their authenticity and original form) to assemble a catalog of Greek medical texts. This undertaking served as the starting point for Alain Touwaide, PhD, later joined by his wife and companion in scientific adventures Emanuela Appetiti, to compile an updated catalog of Greek medical manuscripts. Published in October 2016 by Routledge Press, *A Census of Greek Medical Manuscripts: From Byzantium to the Renaissance* is the culmination of 30 years of travel, research, and discovery.



Touwaide's efforts have expanded the original catalog of Greek medical texts by more than 50%, and *Census* includes manuscripts with texts that delve into the practice of dream interpretation, herbal medicine, diet, and planting calendars. In Touwaide's own words, he listed any text with the common point of "the care of human health" (oral communication, December 2, 2016).

Touwaide explained: "[The Greek] concept of medicine is much closer to what is now integrative medicine. For them, human health and, by consequence, also disease … is the result of the interaction between the environment and the individual." Therefore, he said, "plants were key" in ancient Greek medical practice.

The subtitle of the work, *From Byzantium to the Renaissance*, serves to date only the manuscripts themselves rather than the information they contain. Many of the manuscripts, though written between 800-1599 CE, contain transcriptions of much older works dating back to Hippocrates, who is considered the "Father of Medicine" and lived and worked in the fifth and fourth centuries BCE.

Extant Greek-language medical manuscripts, however, tell only part of the story. They reference some works that have been lost to historians, or perhaps exist in another part of the world, copied into another language. "Much of the Greek scientific literature has been translated into Arabic, and also into Georgian, Armenian, Slavic languages, Coptic — all these languages of the Near East," Touwaide said. "Many of these texts … have been preserved in these other languages while we don't have them in Greek."

The time period covered by *Census* includes the rise of the Byzantine Empire, which grew in prominence from a Roman settlement to a powerful political entity in its own right after the fall of the Roman Empire in the fifth century CE until it was conquered by the Ottoman Empire in 1453.

At its peak, the Byzantine Empire included much of the land surrounding the Mediterranean, and its capital, Constantinople (now Istanbul, Turkey), became one of the largest and wealthiest cities in Europe. Also known as a city of learning, it contained the University of Constantinople and the Imperial Library, which is said to have housed more than 100,000 volumes at its peak. It was at this university and library that many of these ancient texts were preserved thanks to key advancements in book production technology: the change to parchment from the more delicate papyrus and the binding of books instead of rolled scrolls.

"There was a revolution in book production that can be compared exactly to what is happening now in the digital world," Touwaide said, comparing the phenomenon to the adoption of digital e-book copies instead of physical copies. "At that time, they changed the way of writing books … and so they converted all the available texts into the new writing, and they abandoned or destroyed whatever book it was in the ancient writing system." These manuscripts followed the people who created them. After the fall of Constantinople in 1453, refugees from Byzantium streamed into Italy, France, and Spain, where scholars and scientists continued


Appetiti (left) and Touwaide (right) examine a manuscript.

Representation of a thistle (*Eryngium* spp., Apiaceae). Manuscript: Pierpont Morgan Library, New York. M 652, 10th century CE.

to produce works in Greek during the Italian Renaissance.

Misconceptions abound regarding the information contained in these manuscripts. "One thing needs to be clear," said Touwaide. "There is an idea that is very much diffused in common culture that these manuscripts were copied by monks in the Dark Ages who didn't know what they were doing…. Manuscripts were not copied exclusively by monks but mostly by physicians. There were no 'dark ages.' These people were by no means in an era of ignorance…. They knew exactly what they were doing." These manuscripts, therefore, give historians and researchers a glimpse of a medical tradition that is more than merely a snapshot of the past. Annotated by physicians sharing their own observations, these texts show the evolution of medicine, care, and treatment in the Greek tradition.

Touwaide compared this ongoing study of the effects of plants to modern clinical trials spanning seven centuries. "Instead of considering that these texts are quackery, superstition, magic, all these kinds of ideas, we should look at them as clinical trials. What we are doing now, even if we do it on 10,000 patients, is without comparison to what we have in the ancient texts," he added. Physicians recorded their observations, kept what worked, and discarded what did not.

Illustration of sage (*Salvia officinalis*, Lamiaceae) from *De materia medica*. National Library in Naples (MS *Neapolitanus olim Vindobonensis graecus* 1). 7th century CE.

Touwaide and Appetiti, both of whom formerly were affiliated with the Smithsonian Institution in Washington, DC, founded the nonprofit Institute for the Preservation of Medical Traditions in 2007 to research traditional medicine in the hopes of creating new advances in the field of modern medicine. In 2010, the Institute collaborated with the Smithsonian's Center for Conservation and Evolutionary Genetics to study the findings of a second-century BCE shipwreck off the coast of Tuscany, Italy, that included intriguing medical equipment among the excavated artifacts.[1] Thought to belong to a physician on board, one of the artifacts was a tin container holding small, circular tablets that resembled pills. Preliminary DNA sequencing performed on the organic contents of the tablets indicated that they contained common edible garden plants: carrot (*Daucus carota*, Apiaceae), parsley (*Petroselinum crispum*, Apiaceae), celery (*Apium graveolens*, Apiaceae), wild onion (*Allium cepa*, Amaryllidaceae), radish (*Raphanus sativus*, Brassicaceae), and cabbage (*Brassica oleracea* var. *capitata*, Brassicaceae), with the possible addition of hibiscus (*Hibiscus* spp., Malvaceae) and yarrow (*Achillea millefolium*, Asteraceae).

All of these plants, Touwaide points out, were mentioned in ancient medical texts as treatments for a variety of complaints. While food was inextricably linked with medicine in ancient practice, this discovery, thus far the only one of its kind, indicates that medicinal preparations were far more sophisticated than simply digging up a plant and eating it in order to obtain its benefits.

A Census of Greek Medical Manuscripts is the culmination of this effort to combine ancient tradition with modern innovation, uncovering previously undocumented manuscripts and texts, and correcting out-of-date information. Incorrect information regarding the location of manuscripts, which can arise when private collections are sold, can lead to confusion for any researcher wishing to examine the original manuscripts.

Touwaide studies a medical manuscript (*iatrosofion*) at the Korai Library on the Greek island of Chios in September 2016.

Monastery of Panagia of Machairas (Cyprus), Manuscript A 18. Photo courtesy of the Leventis Foundation, Cyprus.

Touwaide and Appetiti visited collections as famous and varied as the Pierpont Morgan Library in New York, the Vatican Library, the British Library, and the Bibliothèque Nationale de France, as well as small, privately owned collections scattered across the globe in order to catalog and identify each manuscript. Additions to Diels' catalog list the title, the author if known, the collection to which the manuscript belongs, and a brief overview of its contents. This information provides immense value to researchers, who can look up a manuscript and know beforehand if it contains subjects relevant to their study.

"*A Census of Greek Medical Manuscripts* is long overdue and most welcomed," wrote John M. Riddle, PhD, Alumni Distinguished Professor Emeritus of history at North Carolina State University and former president of the Society for Ancient Medicine and the American Institute for the History of Pharmacy (email, November 14, 2016). "On top of that, the fact that a scholar such as [Touwaide] undertook and successfully completed an arduous, painstaking, and expensive task makes the book's appearance all the more meaningful."

The work of decades for Touwaide and Appetiti serves as an invaluable resource for classical scholars around the world, in the tradition of Diels and his original catalog. As medical science draws increasingly on natural products research for new sources of drugs, perhaps the knowledge recorded by ancient Greek physicians holds the key to the next big discovery. HG

—Hannah Bauman

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Results of New Cranberry Trial in *JAMA* Misreported to the Public

Inaccurate media reports suggest that cranberry has no value in preventing urinary tract infections

Reviewed: Juthani-Mehta M, Van Ness PH, Bianco L, et al. Effect of cranberry capsules on bacteriuria plus pyuria among older women in nursing homes: A randomized clinical trial. *JAMA*. 2016;316(18):1879-1887. doi: 10.1001/jama.2016.16141.

On October 27, 2016, the *Journal of the American Medical Association* (*JAMA*) published online a randomized, double-blind, placebo-controlled clinical study by Juthani-Mehta et al. from the Yale School of Medicine.[1] The trial was designed to evaluate the effects of a cranberry (*Vaccinium macrocarpon*, Ericaceae) juice extract preparation on bacteriuria plus pyuria (the presence of bacteria and pus in the urine, respectively) in elderly female nursing home residents. The authors reported that administration of two capsules of a standardized cranberry extract (Ellura capsules, each containing 36 mg proanthocyanidins [PACs]; Pharmatoka; Rueil-Malmaison, France) for 12 months failed to provide a statistically significant difference in the percentage of patients with bacteriuria and pyuria compared to placebo. The authors also did not find any statistically significant differences in the secondary outcome measures, which included symptomatic urinary tract infections (UTIs), mortality, number of hospitalizations, presence of multi-drug-resistant bacteria in the urine, antibiotic treatments for suspected UTIs, and total antimicrobial pharmaceutical drugs administered.

The study results were covered, often uncritically, by major media outlets. For example, an article in *The New York Times* titled "The Cure for UTIs? It's Not Cranberries" inaccurately generalized the results of the study with its misleading headline.[2] The study did not look at the effects of the cranberry extract preparation to cure, or even treat, existing UTIs, as the *Times* headline suggests, but rather at its efficacy in the prevention of bacteriuria and pyuria in older women.

According to data published by the same research group, 25-50% of women living in nursing homes suffer from bacteriuria.[3] Since clinical trials evaluating conventional antibiotic treatments have not shown a reduction in urogenital infection-related diseases and deaths, the current medical practice guidelines for institutionalized adults do not recommend antibiotic treatments for bacteriuria or non-specific UTI symptoms because of escalating antibiotic resistance.[4,5] Due to previous clinical trials that have shown positive outcomes for cranberry preparations in preventing the incidence and recurrence of UTIs, cranberry is seen as a potential alternative to low-dose antibiotics for UTI prevention.

The *JAMA* clinical study included 185 women aged 65 or older who lived in 21 nursing homes in the New Haven, Connecticut, area. The women had to speak English, have lived in the nursing home for at least four weeks, have a life expectancy of more than one month, and be able to provide a clean-catch urine sample. Exclusion criteria included the following: the women could not be on anti-infective therapy for recurrent UTIs, be undergoing dialysis for end-stage renal disease, be taking warfarin, have a history of kidney stones, have a bladder catheter, or be allergic to cranberry. In-service nurses were trained to collect appropriate urine samples in order to have valid results. Urine samples were evaluated every two months for the presence of bacteriuria (at least 100,000 colony-forming units of one or two types of bacteria per mL of urine) and pyuria (any presence of white blood cells in the urine).

From the 185 women that started the study, a follow-up after 12 months for the presence of bacteriuria and pyuria was possible for only 90 subjects; patients were lost due to protocol-unrelated deaths, transferral to hospice care, or development of urinary incontinence. While urine analyses after four and six months showed lower bacteriuria in the treatment group, the trend was reversed in the last six months of the study, but without reaching statistical significance at any time period. During the study period, a total of 350 UTIs were suspected, but only 22 (10 in the treatment group and 12 in the placebo group) were confirmed as symptomatic UTIs. The number of hospitalizations, presence of multidrug-resistant bacteria, antibiotic treatments for suspected UTIs, and total antimicrobials administered all trended in favor of the cranberry treatment, but the differences were not statistically significant. No treatment-related serious adverse events were observed. The frequency of protocol-related non-serious adverse events, including altered mental status, gastrointestinal discomfort, oral cavity issues, skin and soft tissue changes, and weight loss, was similar in both groups.

The authors concluded that cranberry administration does not reduce the occurrence of bacteriuria in older women living in nursing homes. However, 30% of the subjects in both arms had asymptomatic bacteriuria at enrollment, and none were treated with antibiotics prior to starting the study. Cranberry has not been consistently effective at reducing existing bacteriuria, as this could be considered a "treatment" effect, which would not be an anticipated result for cranberry. Strengths of this included the use of a standardized cranberry product, compliance with the dosage regimen, and use of objective criteria to evaluate treatment success. Shortcomings included the

inability to obtain urine samples from many women as the study progressed due to subjects' physical and mental impairments, the lack of an anti-adhesion* test, and the inability to assess the efficacy of cranberry supplementation in women with a history of recurrent UTIs.

Previous clinical trials have shown cranberry to be mainly effective in the prevention of *recurrent* UTIs,[6-10] so the lack of benefits in this study may not come as a surprise since only 1% of the participants in the treatment group had three or more UTI episodes in the 12 months prior to enrollment. This clinical study suggests that there is no benefit to using cranberry to prevent the presence of bacteriuria in this particular population, but a number of recent clinical trials carried out with cranberry extracts provides evidence that cranberry does have a place in the therapeutic arsenal to prevent recurrent UTIs and radiation-induced cystitis.[11]

As such, the suggestion to "move on from cranberries," as stated in a *JAMA* editorial[12] by Lindsay E. Nicolle, MD, a professor in the department of internal medicine and medical microbiology at the University of Manitoba, is not supported when scientific evidence from all published clinical trials is taken into account. Results cannot be extrapolated beyond a negative effect of cranberry on the prevention of bacteriuria. This opinion was echoed by Kalpana Gupta, MD, an associate professor of medicine at Boston University School of Medicine, who commented that she is "not ready to walk away from cranberries," and that "some women with recurrent UTIs may still want to discuss cranberry treatment with their doctors."[2]

Concerns about the validity of the data also were raised in a statement issued by the Cranberry Institute, an organization dedicated to supporting research on cranberries and promoting cranberry health benefits, and in a letter written by Amy Howell, PhD, associate research scientist at the Philip E. Marucci Center for Blueberry and Cranberry Research and Extension at Rutgers University.[13,14] Both statements listed characteristics of the clinical study design and results that do not support the conclusions expressed in Nicolle's editorial. HG

—Stefan Gafner, PhD

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The study results were covered, often uncritically, by major media outlets. For example, an article in *The New York Times* titled "The Cure for UTIs? It's Not Cranberries" inaccurately generalized the results of the study with its misleading headline.

* Anti-adhesion refers to the ability of cranberry PACs to inhibit bacterial adherence to the mucous membranes of the urinary tract. Anti-adhesion is one of the mechanisms by which cranberry exerts its benefits.

Hops Extract Reduces Body Fat in Overweight Subjects

Reviewed: Morimoto-Kobayashi Y, Ohara K, Ashigai H, et al. Matured hop extract reduces body fat in healthy overweight humans: a randomized, double-blind, placebo-controlled parallel group study. *Nutr J.* March 9, 2016;15:25. doi: 10.1186/s12937-016-0144-2.

Editor's note: *This study was sponsored by Kirin Company, Ltd. (Yokohama, Japan), a beverage company with a brewery division. Nine of the study authors are employees of the company.*

Obesity is on the rise worldwide and is associated with an elevated risk of developing metabolic diseases such as diabetes and cardiovascular disease. Dietary changes, including the addition of functional foods with certain bioactive properties, and other lifestyle modifications are recommended to address this condition. Hops, the flower heads of the hop (*Humulus lupulus*, Cannabaceae) plant, are traditionally used in the beer-brewing process to add bitterness and flavor. When stored, hops produce bioactive matured hop bitter acids (MHBAs), which have been shown to decrease body fat in animal models. This randomized, double-blind, placebo-controlled, parallel-group trial investigated the impact of a mature hop extract (MHE) on body fat in healthy, overweight subjects.

Hops *Humulus lupulus*
Photo ©2017 Steven Foster

The trial was conducted by TTC Co., Ltd. (Tokyo, Japan), a contract research organization, from May 2014 to December 2014. Included subjects had a body mass index (BMI) of at least 25 but less than 30 kg/m^2. Subjects were excluded from the study if they were on a diet, used pharmaceuticals or dietary supplements to treat body fat or lipid metabolism, regularly consumed hop-containing foods or excessive alcohol, had one or more systemic diseases or abnormal blood work, or were pregnant or lactating, among other criteria.

To create the MHE, the authors aged 300 g of hop pellets (Hopsteiner GmbH; Mainburg, Germany) for 120 hours and then extracted with warm water for one hour. After several filtration steps, the resultant MHE was standardized to 18.3% MHBAs. The material in the trial consisted of 350 mL of MHE test beverage (containing 35 mg of MHBAs) or placebo beverage. The study authors do not describe the contents of the placebo, but mention that it matched the MHE preparation in taste and appearance. The energy (kcal), carbohydrate, and fiber contents of the MHE beverage and placebo also were matched.

From a total of 511 subjects screened, 200 were randomly assigned (100 men and 100 women) to either the treatment group or the placebo group. Subjects consumed either the MHE drink or placebo beverage once daily for 12 weeks and returned for a follow-up visit four weeks after the test period ended. Study visits occurred at baseline, four, eight, and 12 weeks of treatment, and at 16 weeks (the follow-up visit). At study visits, the MHE or placebo drink was consumed after physical parameters were measured. Subjects completed a lifestyle questionnaire during the screening period, and they were encouraged to maintain their lifestyle throughout the study. They were also instructed to avoid alcohol the day before study visits and to fast beginning at 10 p.m. the night before clinical visits.

Body weight, body fat ratio, waist and hip circumference, systolic and diastolic blood pressure, and pulse rate were measured at each visit. Abdominal fat area was measured with a computerized tomography (CT) scan at baseline, eight, 12, and 16 weeks. Blood and urine parameters were assessed, and subjects kept a daily diary recording their food intake, steps taken (measured using a pedometer), and other physical activity. Baseline parameters were not significantly different between groups. The primary endpoint was any decrease of abdominal fat, with secondary endpoints being changes in other physical parameters. Subjects reported any adverse side effects to the investigators.

The treatment group had a significant decrease in energy intake at the 16-week time point compared to baseline (1,728.5 ± 46.3 vs. 1,810.1 ± 50.9 kcal/day, respectively; $P < 0.05$). However, the treatment group's decrease in energy intake was not significantly different than that of the placebo group at week 16 (1,769.7 ± 45.7 kcal/day). The treatment group's fiber intake also decreased after four weeks compared to baseline (9.98 ± 0.34 g/day vs. 10.79 ± 0.47 g/day, respectively; $P < 0.05$).

In both groups, visceral fat area (VFA) and total fat area (TFA) significantly decreased after 12 weeks compared to baseline ($P < 0.01$ for both VFA and TFA in both groups). The VFA and TFA of the MHE group were significantly less than those of the placebo group after 12 weeks ($P < 0.05$ for both VFA and TFA). Subcutaneous fat area (SFA) also decreased significantly in both groups after 12 weeks compared to baseline ($P < 0.01$ in both groups), but there was no significant difference in SFA between groups at any time point.

Following four, eight, and 12 weeks of treatment, the body fat ratios of those in the treatment group were significantly less than those of the placebo group ($P < 0.05$ at each time point). Body weight and BMI were significantly lower in the treatment group compared with the placebo group after four weeks ($P < 0.01$ for both). In addition, body weight and BMI in the treatment group were significantly decreased after 16 weeks compared to baseline ($P < 0.01$ for both), with no significant changes in the placebo group. Waist and hip circumference also were significantly smaller in the treatment group after four weeks compared to placebo ($P < 0.05$ for both).

In the placebo group, systolic blood pressure was significantly higher after 16 weeks compared to baseline ($P < 0.05$). In the treatment group, pulse rate was significantly slower after 16 weeks compared to the placebo ($P < 0.05$).

Adverse side effects were reported by 47 subjects in the treatment group and 43 subjects in the placebo group, with the most common one being cold-like symptoms. None of the effects were determined to be associated with the test material.

This study demonstrated that the consumption of MHE decreased fat accumulation in overweight subjects. Also, energy intake was significantly decreased in those taking MHE, which suggests that appetite suppression may be involved. The appetite-suppressing effects may be linked to the MHE's bitter compounds, which have been shown to impact appetite and satiety by acting on the gastrointestinal tract. It is suggested that future studies should have a longer duration. This study had significant placebo effects, the reasons for which were unclear to the authors. Also, the average energy intake of the study subjects in Japan was low compared to average energy intake in Western societies. Despite this, MHE may be useful for weight loss. HG

—Amy C. Keller, PhD

Ashwagandha Root Extract Improves Symptoms of OCD in Certain Patients

Reviewed: Jahanbakhsh SP, Manteghi AA, Emami SA, et al. Evaluation of the efficacy of *Withania somnifera* (ashwagandha) root extract in patients with obsessive-compulsive disorder: a randomized double-blind placebo-controlled trial. *Complement Ther Med*. 2016;27:25-29.

Obsessive-compulsive disorder (OCD), characterized by stressful, repetitive, and intrusive thoughts or obsessions followed by actions or compulsions, is thought to be linked to a defect in the serotonergic system. Selective serotonin reuptake inhibitors (SSRIs) are commonly used to treat OCD, but they are considered only mildly effective, with a reported 40-60% of patients failing to respond. Those who do respond to SSRI treatment tend to show only minor improvements in OCD symptoms.

In traditional Ayurvedic herbal medicine, ashwagandha (*Withania somnifera*, Solanaceae) is considered a rejuvenating and revitalizing herb. Its roots, which are used to enhance mental and physical health, have anxiolytic and antidepressant properties and have been used in the treatment of nervous disorders. The phytochemicals thought to play a role in these therapeutic effects include bioactive steroids (withanolides and withanolide glycosides) and alkaloids (withanine and somniferine). In addition, a previous study in mice found that ashwagandha may affect serotonergic transmission. The goal of this randomized, double-blind, placebo-controlled trial was to test the efficacy of ashwagandha root extract as an adjunct therapy for OCD.

Ashwagandha roots were collected in Saravan, Iran, in August 2013. The extract was prepared at the industrial pharmacy lab at the School of Pharmacy at Mashhad University of Medical Sciences in Mashhad, Iran. The roots were dried and powdered, then percolated with 70% ethanol. The resulting extract was evaporated under pressure and freeze-dried to yield a fine powder. The researchers filled 250-mg capsules with either a mixture of 30 mg of the powdered extract and lactose (an excipient) for the treatment group or lactose only for the placebo group.

The study was conducted between March 2015 and September 2015 at the Mashhad University of Medical Sciences. Thirty patients met the following inclusion criteria and were enrolled in the study: diagnosis of OCD per the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision* and current treatment with SSRIs. Patients were randomly assigned to the treatment group (n = 15; one male and 14 females) or the placebo group (n = 15; two males and 13 females). To avoid potential adverse gastrointestinal effects, the patients in the treatment group were instructed to take one capsule daily and increase the dosage by one capsule every four days until they were taking four capsules daily (adding up to 120 mg of extract). At the end of six weeks, the treatment was decreased in the same manner.

The severity of OCD symptoms was assessed in all patients using the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) symptom checklist, a 10-question scale with scores ranging from 0 (no symptoms) to 40 (extreme symptoms). Each patient completed the Y-BOCS checklist at baseline and after six weeks of study intervention.

Ashwagandha *Withania somnifera*
Photo ©2017 Steven Foster

From baseline to the end of the study (six weeks), the median Y-BOCS score decreased from 26 to 14 in the treatment group and from 18 to 16 in the placebo group, a significant between-group difference ($P < 0.001$). At baseline, seven patients in the treatment group and five in the placebo group suffered from comorbid anxiety disorders (i.e., they had one or more anxiety disorders in addition to OCD). The patients in each group were divided into those with comorbid anxiety disorders and those without, and the average reduction of Y-BOCS scores for these subgroups was compared. In both groups, the average reduction of Y-BOCS scores in patients with comorbid anxiety disorders was not significantly different from patients without anxiety disorders. No adverse effects were reported in either group during the study.

According to the authors, this study is the first attempt to investigate the effects of ashwagandha root extract in patients with OCD. Based on the results of this study, the authors concluded that "*W. somnifera* extract may be beneficial as a safe and effective adjunct to SSRIs in the treatment of OCD."

Acknowledged limitations include the study's small sample size, short duration, and lack of a phytochemical analysis of the extract, which could have helped identify the active constituents associated with the observed beneficial effects. In addition, due to the study design, the researchers were unable to determine if the observed anti-obsessive effects were dose-dependent. Unfortunately, there was also a large difference in baseline symptom severity (per the Y-BOCS scores) and the number of patients taking clomipramine or valproate sodium between the treatment and placebo groups. For these reasons, the results of this study should be interpreted with caution. HG

–Shari Henson

Flax Seed and Chamomile Flower Infusion Relieves Dry Mouth in Elderly Patients

Reviewed: Morales-Bozo I, Ortega-Pinto A, Rojas Alcayaga G, et al. Evaluation of the effectiveness of a chamomile (*Matricaria chamomilla*) and linseed (*Linum usitatissimum*) saliva substitute in the relief of xerostomia in elders [published online January 14, 2016]. *Gerodontology*. March 2017;34(1):42-48.

Xerostomia, a condition commonly known as dry mouth, can be caused by a variety of factors, including systemic conditions (e.g., diabetes mellitus and rheumatoid arthritis), mouth breathing, local radiotherapy, and use of tobacco (*Nicotiana tabacum*, Solanaceae) or certain prescription pharmaceuticals. Aging also causes dry mouth due to decreased saliva production and reduced mucin expression from epithelial cells. In the elderly, dry mouth is a permanent, progressive condition that adversely affects quality of life. Saliva substitutes are often recommended and work by temporarily lubricating the mouth.

Chamomile (*Matricaria recutita* syn. *M. chamomilla*, Asteraceae) flower extract has been shown to help reduce oral discomfort and mucositis (mucous membrane inflammation) in patients, and flax (*Linum usitatissimum*, Linaceae) seed produces a water-soluble mucilage that can hydrate the mucosa. The purpose of this randomized, double-blind, crossover study was to evaluate a saliva substitute made of chamomile flower and flax seed for older patients with dry mouth.

Patients over the age of 60 who had dry mouth were recruited in Santiago, Chile, from the University of Chile School of Dentistry and the Health Reference Centre of Peñalolén Cordillera Oriente. Patients with oral mucosa lesions, oral motor disorders, or cognitive limitations were excluded from the study.

For one week, patients (N = 74; mean age = 66.7 ± 6.47 years) were treated with either 2 mL of a commercial carboxymethyl cellulose-based saliva substitute (Farmacias Ahumada; Santiago, Chile) or 2 mL of an herbal preparation made by the study authors (an infusion of 30 g of flax seed and 1 g of chamomile flowers in one liter of water) four times per day. After a one-week washout period, the patients switched to the other treatment. Before and after each treatment phase, the severity of dry mouth symptoms was measured by a 10-point visual analog scale (1 = absence of symptom, 10 = "maximum imagined symptomatic perception"). The primary endpoint was the change in symptoms of dry mouth from baseline to treatment end.

Nearly all (92%) of the patients were women. At baseline, 45% of the patients had a salivary flow of 0.2 mL or less per minute (hyposialia), and 55% had normal flow (between 0.2 and 1.0 mL per minute). The authors reported the following dry mouth-related factors in the study participants: disease (arterial hypertension, "depressive symptoms," and arthritis were the three most common conditions), medication use, smoking, and maxillofacial radiation. At baseline, 59.5% of the patients had a sensation of thick saliva, 27% had a sensation of "burning tongue," 54.1% needed to drink liquids to swallow, and 56.8% had difficulty swallowing food.

Chamomile *Matricaria recutita*
Photo ©2017 Steven Foster

Compared to baseline, the herbal saliva substitute significantly improved dry mouth (P = 0.003), sensation of thick saliva (P = 0.028), sensation of burning tongue (P = 0.038), and difficulty in swallowing food (P = 0.001). The conventional saliva substitute significantly improved only two symptoms: dry mouth sensation (P = 0.002) and needing to drink liquids to swallow (P = 0.019), compared to baseline. The herbal saliva substitute was significantly more effective than the conventional saliva substitute at decreasing symptom severity of dry mouth (P = 0.022), sensation of thick saliva (P = 0.048), and difficulty in swallowing food (P = 0.001).

The authors conclude that the herbal saliva substitute improved more symptoms than the conventional treatment. Limitations of the study include the short treatment duration (especially given the chronic nature of dry mouth in elderly individuals), the unequal gender ratio of participants, and the lack of reported adverse side effects (if any). The safety of long-term use of this herbal treatment should also be evaluated. "The Chilean elderly population has a natural relation with these herbaceous plants by frequently using them as food additives or as teas," the authors note. Therefore, they suggest that the chamomile-flax herbal preparation, which is inexpensive and can be made at home, may be an appealing option in Chile, where treatments for dry mouth are limited. HG

—Heather S. Oliff, PhD

Flax *Linum usitatissimum*
Photo ©2017 Steven Foster

MEDICINAL FUNGI

Chemistry, Activity, and Product Assurance

By Christopher Hobbs, PhD, LAc

Turkey tail *Trametes versicolor*
Photo ©2017 Jerzy Opiola

Considering the total estimated number of fungal species (about 5.1 million),[1] it is no surprise that among them are species that produce important compounds (e.g., penicillin) that form the basis of several classes of medicinal products, such as antibiotics and immune-enhancers, as well as some species that are a danger to human health (e.g., *Aspergillus* and *Candida* species).[2]

Mushrooms, such as reishi (also known as *ling zhi*; *Ganoderma lucidum*, Ganodermataceae), have been used medicinally in Asia for centuries.[3,4] Complementing this rich history of use, numerous scientific studies have been performed on mushroom extracts for their potential health benefits. Many of these studies have been performed using cell culture assays and animal models,[5,6] but there is a growing body of evidence from human clinical trials as well.

For example, results from human clinical trials suggest that mushroom preparations may be beneficial as a supportive part of cancer care. Researchers from Japan have found that certain mushroom extracts may help improve the quality of life and five-year survival rates of patients with gastrointestinal cancers undergoing chemotherapy.[7,8] The first US National Institutes of Health (NIH)-funded phase 1 studies of the anticancer and immune-supportive effects of fungal preparations in patients with breast cancer also have shown positive results.[9] Another trial found that women taking a turkey tail (*Trametes versicolor*, Polyporaceae) preparation after standard chemotherapy and radiotherapy had improved immune status compared with those receiving standard care alone.[10]

More clinical trials are needed to answer some of the basic questions that arise regarding medicinal mushroom preparations, such as which species are the most effective for a certain condition, the optimal extraction methods to retain as much biological activity as possible, and the appropriate dose and dosage for a wide variety of patients. Still, results from human clinical trials of mushrooms have been promising, and this growing research base has helped ignite interest in fungi-based products in the dietary and food supplement industry in the United States and other countries.

Fungal Constituents

The cell walls of fungi are complex and dynamic, and their constituent parts depend on environmental conditions and genetic factors. Most fungal cell walls are made up of more than 90% polysaccharides,[11] a class of compounds that includes α-glucans and β-glucans, among others. Fungal glucans have been the subject of a considerable amount of research, and extensive pharmacokinetic, in vitro, in vivo, and human studies are available in the literature.[12]

β-Glucans

The most-studied fungal components are the β-glucans and β-glucan complexes — formations of β-glucans and other molecules, such as proteins, fatty acids, and chitin, which add toughness and flexibility to the cells. β-glucans and β-glucan complexes compose up to 50% (by dry weight) of the cell walls.[11,13]

β-glucans are simply glucose polymers with the glucose molecules attached in a specific manner (branched or unbranched). β-glucans are named according to the location of the bonds that hold together the chain of glucose molecules (Figure 1). For example, "1,3-β-D-glucan" indicates a polysaccharide consisting of a chain of β-D-glucose* molecules linked by bonds at the first and third carbon atoms.

In fungal species, 1,3-β-glucans occur with varying degrees of branching and with side chains attached at various points (Figure 2). Both 1,3-β- and 1,6-β-linkages are present in fungal species — a characteristic unique to fungi — but the style of branching and spatial architecture vary considerably from species to species.[13-15] In basidiomycetes and ascomycetes (the two main groups of medicinal fungi), the main central scaffolding of the cell wall is made up of 1,3-β-glucans and 1,3:1,6-β-glucans bound to chitin and chitosan by 1,4 linkages.[16,17]

* For simplicity, the "D" will henceforth be omitted in the names of glucose molecules and glucan compounds. The letter indicates an isomer of glucose (i.e., a glucose molecule with a specific spatial arrangement of its atoms).

The chemical structures and spatial arrangements of β-glucans can have an impact on various properties of the compounds. Some β-glucans are soluble in water, and some are not, depending on the number and character of the branches.[18] Fungal β-glucans (both linear 1,3-β-glucans and branched 1,3:1,6-β-glucans) have tertiary structures, such as the triple helix structure, which has been linked to increased biological activity.[14,19]

β-glucans and β-glucan complexes have shown immune-stimulating effects[20] and a high level of safety.[21] Recently, there has been an explosion of research interest in the role of β-glucans from fungi, including yeasts, in human adaptive

Figure 1. The β and α orientations of glucose molecules with numbered carbon atoms. (via Wikipedia)

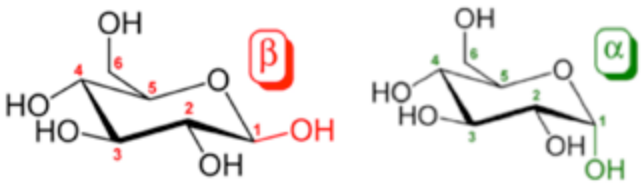
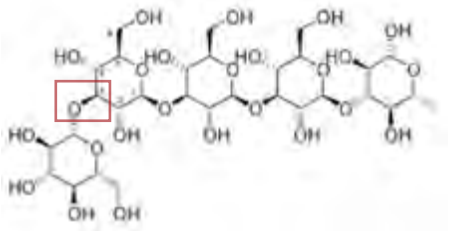
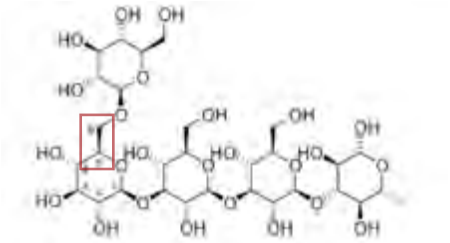


Figure 2. Examples of various types of β linkages. (via Wikipedia)

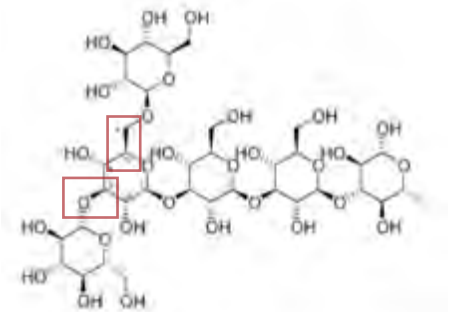
1,3-β linkage



1,6-β linkage



Glucan containing both 1,3-β- and 1,6-β-linkages†



† For simplicity, glucans containing both 1,3-β- and 1,6-β-linkages will be referred to as "1,3:1,6-β-glucans" throughout the article.

Reishi *Ganoderma lucidum*
Photo ©2017 Steven Foster

immunity.[22-24] Over hundreds of millions of years, animals and plants have developed exquisitely evolved sensing and response pathways to fungi.[24] The ability to sense fungi cell wall components, such as 1,3:1,6-β-glucans, is facilitated by specific receptors (e.g., dectin-1 receptors in the gut and on immune effector cells like macrophages[25,26]), a process that is necessary for protective fungal-mediated immunomodulation.[27]

Besides the glucan-chitin complexes, cross-linked proteins form part of the structural matrix throughout the fungal cell wall.[28] The outer portion of the cell walls are composed mostly of mannans and glycoproteins, which are the most important antigenic components of fungi. (An antigenic component enables the organism sensing fungal glucans to produce an immune response, especially through the production of antibodies.) However, the immunomodulating effects of fungi after ingestion by vertebrates and invertebrates likely are due primarily to the β-glucan polymers, as they are not found in animals.[29] This process (i.e., animal immune cells recognizing fungal β-glucans as "foreign" and thus producing an immune response) is known as innate pathogen-associated molecular pattern (PAMP) recognition.

Lion's mane *Hericium erinaceus*
Photo ©2017 Lebrac

α-Glucans

α-glucans are the other well-known glucans in plants and fungi. Examples of α-glucans include structural fibers (e.g., 1,3-α-glucans that are often attached to 1,3:1,6-β-glucans[40]), starch (a 1,4-α-glucan), and the glucose storage molecule glycogen (which contains 1,4-α- and 1,6-α-glucans).

Amylose, a component of starch, is known to be present in small quantities in the spores of some fungal species, presumably for blocking oxygen uptake to slow metabolism and prolong survival.[41] Glycogen is a highly branched energy storage molecule that is similar to animal glycogen and is present in fungal cells at levels of 5-10%[42,43] and up to 18% in some fungi as an energy source for sporulation.[44]

These α-glucans are ubiquitous in the plant and fungi kingdoms and have not shown to be as biologically active as the β-glucans specific to fungi and yeasts.[45]

Low-Molecular-Weight Compounds

Fungi also contain a variety of low-molecular-weight compounds, such as terpenes, phenolic compounds, alkaloids, fatty acids, and proteins. These compounds are found mostly in the cytoplasm within the cell wall. Well-known low-molecular-weight compounds include terpenes from reishi, phenolic hericenones from lion's mane (*Hericium erinaceus*, Hericiaceae), cordycepin from *Ophiocordyceps sinensis* (Ophiocordycipitaceae) and *Cordyceps militaris* (Clavicipitaceae), and many other compounds.[6]

Knowledge of low-molecular-weight chemistry in fungi is still incomplete, since nearly all the evidence for biological activity comes from preliminary in vivo and in vitro studies. However, considerable research has been published on some low-molecular-weight compounds, particularly the triterpenes that are key components of reishi.[46]

Mycelia vs. Fruiting Bodies: Differences and Considerations

According to records from centuries-old herbals and pharmacopeias, fungal products throughout history have

Species Recognition: Fungal β-Glucans Are Like Name Tags to Other Species of Plants, Animals, and Microorganisms

Considerable work has been done to characterize the β-glucan molecules in fungi using conventional methylation techniques, as well as ^{13}C-NMR (carbon-13 nuclear magnetic resonance) spectroscopy, which allows for the identification of carbon atoms for structure elucidation.[30] This research has yielded specific data on the branching patterns in various 1,3-β-glucans. Branched 1,3:1,6-β-glucans — in addition to mannans and glycoproteins[31-33] — are thought to play a role in species recognition among individuals of different strains and clonal lineages of one species, or between other species of fungi,[34] as well as between plants and fungi,[35,36] and between animals (including humans) and fungi.[37-39] This recognition is ancient, has developed over evolutionary time, and can trigger a complex immune response in humans.[37]

been produced primarily from the actual mushroom (i.e., the "fruiting body" or sporocarp, which is a special, morphologically distinct reproductive structure produced by each fungal species).[3] The medicinal uses of at least 10 different fungal fruiting bodies in the Eastern Han Dynasty (25 CE to 220 CE) were mentioned in Shen Nong's herbal classic.[47] There is also documentation of the cultivation of some species. For example, the cultivation of wood ear (*Auricularia auricula-judae*, Auriculariaceae) and shiitake (*Lentinula edodes*, Omphalotaceae) — both of which are grown on wood for their fruiting bodies[48] — was first mentioned as early as 600 CE and 1000 CE, respectively.

Today, many commercial products are made from the mycelium,‡ the vegetative part of fungi, primarily for its cost-effectiveness and convenience. (The dominant phase of fungi is known as the mycelial or vegetative phase.) Mushroom mycelium of many species can be grown rapidly on sterilized grains such as rice (*Oryza sativa*, Poaceae) with less effort and cost than collecting fruiting bodies from the wild or cultivating fruiting bodies, the formation of which requires waiting for ideal conditions when grown on grain or other substrates. In cultivation trials of *Pleurotus* spp. (Pleurotaceae) grown on leftover beer grains (a protein- and nutrient-rich mixture that contained additives such as wheat [*Triticum aestivum*, Poaceae] bran), researchers reported a fruiting body conversion efficiency of approximately 19% — the highest efficiency found among tested substrates.[49] Comparatively, grain-grown mycelia used in dietary supplements provide manufacturers with roughly 40-95% biomass utilization, depending on the amount of mycelia and substrate in the finished product. This is because all the mycelium and substrate is harvested, heated, dried, ground, and encapsulated.

Chemical and Pharmacological Differences

Mycelia have been reported to possess a similar array of active compounds as the corresponding fruiting bodies.[51-53] However, some researchers have found higher levels of β-glucans in the fruiting bodies of tested species. Using a calorimetric method, researchers found 3.7 times more 1,3:1,6-β-glucans and 2.3 times more total β-glucan content in the fruiting bodies of shiitake than in the mycelium of the same species. In general, total β-glucan content was higher in the fruiting bodies of other tested species as well, with the exception of the common button mushroom (*Agaricus bisporus*, Agaricaceae), which contained more β-glucans in the mycelium than in the fruiting bodies.[54]

Even within the same species, the structure of β-glucans in the fruiting body may differ from the structure of β-glucans in the mycelium. Calonje et al. (1996) found

‡ "Mycelium," in the singular form, refers to masses of mycelium of one species or strain. The plural form, "mycelia," refers to batches or masses of mycelium of more than one species or strain.

Turkey tail *Trametes versicolor*
Photo ©2017 Chris Hobbs

Turkey Tail Preparations: PSK and PSP

The turkey tail preparation polysaccharide-K (PSK, a protein-bound polysaccharide) was first produced in the early 1970s in Japan.[50] Both PSK and polysaccharide peptide (PSP, a similar turkey tail product from China) are derived from the mycelium of turkey tail, but the process by which these products are made is not comparable to current products from mycelia grown on grain. PSK and PSP are products derived from pure mycelium grown on nutrient solutions (submerged cultures) that produce a mycelial mass with no other substrate or organisms present in the finished product. The glucans, protein-bound glucans, and other non-starch polysaccharides are then highly purified by a series of extraction steps that involve alkaline solutions.[50]

PSK and PSP are characterized by their β-glucan contents and have been shown to have immunomodulatory and anticancer effects. These active, high-molecular-weight complexes are the most-researched medicinal fungi products worldwide, with many clinical trials (at least 37 trials have been conducted on the protective effects of PSK) and in vivo and in vitro research studies published.[9] β-glucans are by far the most widely characterized and studied fungal components of PSK and PSP. PSK and PSP are still widely available for sale in Asia, the United States, and other countries. However, they are very expensive because of the extra processing required, name recognition, and clinically demonstrated efficacy and safety for supporting immunity in people with various forms of cancer.

"striking differences" in sugar linkages and the conformations (spatial arrangements) of β-glucan polysaccharides between the fruiting bodies and mycelium of the same strain of *A. bisporus*.[55] Such structural differences may be due in part to the varying media upon which the mycelium is grown.[20,56]

More studies are needed to answer clearly for each medicinal species whether the fruiting body or the mycelium has consistently higher levels of active compounds, and how certain variables (e.g., growing conditions and other factors) may influence these levels.

Comparing Biological Activity

One recent study[57] examined the biological activities of different types of medicinal mushroom products purchased from natural health food stores in the United States. A majority (60%) of the 39 tested products contained ground fungi (mostly mycelia on grain) rather than hot-water extracts or steam-heated mushroom powders. The researchers found that the hot-water extracts had significantly higher immunological activity (as determined by the activation of toll-like receptor 2 [TLR2], an immune receptor) and "immune-enhancing potential" (as determined by the induction of tumor necrosis factor-α [TNF-α], an immunochemical) than the products containing ground, raw fungal material. This preliminary study suggests that heating (and perhaps concentrating) the fungal material increases TNF-α activity in lab cultures, and does not neccesarily imply better clinical outcomes.

Researchers have discovered other receptors that bind fungal polymers on a variety of immune effector cells, such as macrophages, neutrophils, eosinophils, and natural killer cells, and on immune tissue in the gut (e.g., dectin-1 receptors and complement receptor 3 [CR3]).[25,58,59] β-glucans binding to these receptors could activate more diverse immune pathways than if they bound to TLR2 only. For instance, it is known that both dectin-1 and toll-like receptors work together to activate macrophage function in response to pathogenic mycobacteria.[60]

In vivo research[61,62] has shown that, after oral administration, large yeast 1,3:1,6-β-glucans bind to receptors (e.g., dectin-1) expressed on the surface of intestinal macrophages. The macrophages then internalize the β-glucans through endocytosis and shuttle them to the spleen, lymph nodes, reticuloendothelial tissues, and bone marrow. Once in the marrow, macrophages degrade the β-glucans and secrete smaller, biologically active products that bind to bone complement receptors (e.g., CR3) of marrow granulocytes, confering an enhanced ability to kill tumor cells. Human macrophages act similarly in response to fungal β-glucans, and dectin-1 receptors strongly enhance immune response to fungal pathogens.[63] However, one recent study indicates that CR3 may be more important for macrophage activation and endocytosis of β-glucans.[64]

While it is true that the fruiting bodies of fungi are in essence made up of densely packed mycelia, the mycelium in a fruiting body is not identical to the mycelium in other stages of growth and development. Lacourt et al. (2002)[65] found significant differences in gene expression in approximately 33% of the genes studied in the whitish truffle (*Tuber borchii*, Tuberaceae) during morphogenesis (i.e., the transformation of the mycelium vegetative phase to a mature fruiting body phase). Expression of glutamine synthetase and glucan 1,3-β-glucosidase, among others, was highly up-regulated. The researchers concluded that amino acid biosynthesis, cell wall synthesis, and other protein syntheses were all strikingly altered during morphogenesis. In *P. ostreatus*, Lee et al.[66] found that only 5.3% of unige-

Button mushroom *Agaricus bisporus*
Photo ©2017 0x010C (WikiCommons)

Close-up image of button mushroom (*Agaricus bisporus*) mycelium
Photo ©2017 Rob Hille

Shiitake *Lentinula edodes*
Photo ©2017 Steven Foster

Potential Health Benefits of Grain in Medicinal Mushroom Products

Grains are a good source of soluble fiber, which is generally beneficial to health. Arabinoxylans, a common component of the walls (bran) of a number of grains, are the main non-starch polysaccharide of most grains.[72,73] In addition to arabinoxylans, brown rice bran also contains phenolic compounds, vitamins, and sterols; its health-giving properties have been widely cited.[74]

Arabinoxylans are modified by gut bacteria (so-called prebiotics) to produce immunologically active compounds. Numerous studies have reported on the immunological and other beneficial effects of rice bran that is fermented by shiitake mushrooms — a process that produces active arbinoxylans and other compounds.[75,76] However, fungal culturing of rice or other grains may not be necessary for the breakdown or creation of immunologically active oligomeric arabinoxylans if the microbes in the human gut can do the same job.[77,78] Most whole cereal grains, particularly brown rice, can provide a significant amount of arabinoxylans in the diet and may serve as a cost-effective source of activated arabinoxylans.

nes were commonly expressed in both stages (out of 1,256 total unigenes identified). Many other authors have reported on the differences in gene expression between the mycelium and the fruiting body of other species, including *L. edodes*.[67,68]

Studies comparing the biological activities of different types of commercial products are rare, and in vitro and in vivo studies do not always translate to activity and clinical benefits in humans.[69] Such results can be taken as a starting point when selecting products that offer the best value, along with other criteria, such as traditional uses, extraction methods, and dosage regimens.

Undigested Grain in Mycelial Products

Given that fruiting bodies and mycelia of fungi species have the potential to produce similar profiles of active compounds, does it make a difference if finished consumer products contain one or the other?

In both theoretical and practical terms, a finished consumer product based on mycelia could potentially contain more starch or glycogen (derived from the undigested grain) and fewer β-glucans than a finished consumer product based on fruiting bodies. Thus, some have suggested that the efficacy and value of commercial medicinal mushroom products may depend on how much of the substrate upon which the mycelium is grown is consumed by the fungus and turned into active compounds, and how much of the product is non-consumed starch and other constituents from the original substrate (or glycogen stored in the mycelia from the rich source of easy-to-metabolize starch in the cooked grain).

However, the potential of the finished cultivated mycelial mass to contain a significant amount of undigested grain after it is harvested, dried, and milled is a point of controversy. Exactly how much grain a mycelium can consume when it is fully grown depends on the strain of fungus and how aggressively it consumes the nutrients, as well as the growing conditions and the time of harvest. Longer culture times will result in more of the grain being consumed by the fungus and more fungal growth, but the fungus begins to terminate the growth process when key nutrients are depleted.

Researchers have investigated the possibility of mycelia cultivated on grains (e.g., cooked rice), resulting in high starch or glycogen concentrations originating from undigested grain in the finished product.[13,70]

In a recent study on β-glucan testing methods,[13] researchers found that of 12 commercial product samples purchased from a natural food market, half of them had 5% or less measurable

β-glucan content. The first two samples were multi-species mycelial blends, and the others were single species (e.g., reishi, cordyceps, or chaga [*Inonotus obliquus*, Hymenochaetaceae]). These six products had α-glucan (starch/glycogen) contents of 66.4%, 72.5%, 83.2%, 64%, 24.1%, and 70%. When unprocessed fruiting bodies of common medicinal species were tested by the same methods, most polypores had much higher β-glucan levels and very low α-glucan levels (hoelen [*Wolfiporia cocos*, Polyporaceae] = 74%/0.8%; reishi = 54%/0.2%), whereas some fleshy species had moderate β-glucan levels but low α-glucan levels (maitake [*Grifola frondosa*, Fomitopsidaceae] = 35%/1.3%; shiitake = 27%/0.9%; oyster [*P. ostreatus*] = 33%/0.4%).

Brauer et al. (2011)[71] reported the percentage of α-glucans (likely glycogen) in shiitake fruiting bodies to be about 2-10%, depending on the spawn source, strain, and environmental conditions under which they were grown. McCleary and Draga (2016)[13] found that the total α-glucan content of 20 mushroom fruiting body samples varied between 0.4% and 3.4%.

Close-up image of oyster mushroom (*Pleurotus ostreatus*) mycelium growing in a petri dish on coffee grounds. Photo ©2017 Tobi Kellner

Oyster mushroom *Pleurotus ostreatus*
Photo ©2017 Charl de Mille-Isles

Quality Control of Medicinal Mushroom Products

Testing for β-Glucans

Based on the extensive literature on the activity, clinical benefits, and safety of fungal β-glucans, a number of tests have been developed to quantify their levels in mycelia, fruiting bodies, and finished preparations.[13] Although other compounds are likely involved in the immunomodulating and anticancer effects of mushrooms, mushroom β-glucans (and complexes of β-glucans, chitin, proteins, and fatty acids) are by far the most studied fungal components in the published literature.[59,86-93]

Acid Hydrolysis/Enzymatic Procedures

McCleary and Draga (2016)[13] evaluated various methods for the analysis of β-glucans in mushrooms and myce-

Starch and Glycogen in Medicinal Fungi Products

Fungal mycelia and fruiting bodies produce α-glucans (starch/glycogen), which are analogous to the starch found, typically at lower levels, in plants. In many fungal species, starch is, at most, a spore coating that regulates water loss. Few studies have detected starch in fungal mycelia or fruiting bodies themselves, and the few that have may have detected glycogen, not starch.

Many fungi contain substantial quantities of glycogen,[79-82] which has been found to be essential for fruiting body formation.[83,84] Since glycogen is structurally similar to starch (in that it has a 1,4-α-glucan linear structure with 1,6-α branches), the measurement and differentiation of starch and glycogen in products can be challenging.[43] However, one study[84] found approximately 3.5% glycogen in *Agaricus bisporus* mycelium grown in submerged culture.

A mycelium grown on grains that have an abundance of starch enables the growing mycelium to build up stores of glycogen as it colonizes and digests the grain. Excess glycogen is stored in the cytoplasm in the form of granules called glycogen microbodies. This has also been shown in mycorrhizal species (i.e., fungal species that have symbiotic relationships with plants) that have access to free sugar from trees. Glycogen storage granules became abundant at the tips of a growing mycelium when food, in the form of starch, was plentiful in the tree cells. This increase in glycogen in the growing mycelium was directly correlated with a decrease in starch in the roots of the tree.[85]

It appears that the "starch" that is cited to be in high concentrations in finished medicinal mushroom products is a mixture of starch and glycogen (or, likely, mostly glycogen) inside the mycelium. The amounts of starch and glycogen depend on the species involved, how thoroughly the mycelium colonizes the substrate, and how much starch it digests. Still, glycogen is not likely to be active as an immunomodulator any more than starch is, and so supplying an overabundance of starch for fungal growth may not be optimum for producing high quantities of active 1,3:1,6-β-glucans. However, more research is needed to clarify this. The conversion of starch to 1,3:1,6-β-glucans is also dependent on the species of fungus and growing conditions.

lial products, including enzymatic procedures and methods involving a combination of both acid hydrolysis and enzymatic procedures. They concluded that the most effective, reliable, and reproducible method across a broad range of mushroom species and mycelial products was the acid hydrolysis/enzymatic procedure. The acid hydrolysis/enzymatic method from Megazyme (as described below) for testing the percentage of β-glucans has been used and published in a number of scientific studies, adding to its credibility.[94-97]

Using this procedure, McCleary and Draga[13] determined the total glucan content (α and β) of various products. First, the fungal mycelium, fruiting body, or finished product was heated in hydrochloric or sulfuric acid to 100°C, breaking all the bonds between glucose molecules in all polysaccharides containing glucose. Enzymes that work specifically on the bonds between glucose molecules were then added to the mixture to make sure all the glucose was released from polymers and in a free form. Separately, specific enzymes that release glucose from starch/glycogen (α-glucan) molecules were blended with the starting test material before acid and heat treatment, breaking the glucose bonds only in starch/glucose and not in any of the β-glucans. Since the acid/heat treatment broke *all* glucose bonds, subtracting the percentage of starch (α-glucan) determined by this enzymatic treatment from the *total* glucose derived from β-glucans and α-glucans gave an accurate percentage of β-glucans in the tested material.[98] Ideally, the accuracy of this method should be confirmed by direct measurement of β-glucans.

Glucan Enzymatic Method Assay

Researchers have also used the glucan enzymatic method (GEM) assay to quantify fungal β-glucans in extracts and formulated products. This process uses the enzyme lyticase, followed by treatment with other enzymes that convert β-glucans to glucose, which is then measured by another enzymatic method.[99] However, the GEM assay seems to underestimate the amount of β-glucans,[13] which likely has to do with the insolubility of approximately 80% of the β-glucans (unless the cell walls are treated with acid to break their bond to chitin and other polymers).[100]

Fungitell Test/Factor G Test

Another published test for fungal β-glucans is also widely used for medical applications. The Fungitell test (Viracor-IBT Laboratories) was approved in 2003 by the US Food and Drug Administration (FDA) for detection of serum 1,3:1,6-β-glucans as a diagnostic tool to confirm invasive fungal infections.[101,102] This quantitative test is based on the *Limulus* factor G test, and is specific only to 1,3-β-glucans. (Factor G is the name of the enzyme that recognizes the 1,3-β-glucans.) Numerous studies have shown the specificity and accuracy of the method.[103]

The factor G-based test also has been used to identify 1,3-β-glucans in mycelium culture supernatants (the nutrient-containing liquid that is separated from the mycelium by centrifugation).[103] Nagi et al. (1993)[104] found that the reactivity of factor G triggered by 1,3-β-glucans was not only

Wood ear *Auricularia auricula-judae*. Photo ©2017 Stu's Images (Wikicommons)

dependent on the amount in the solution being tested, but also on the conformation of the 1,3-β-glucans (single helix, triple helix, etc.).

Odabasi et al. (2004)[105] found that factor G-based tests such as the Fungitell test could not differentiate β-glucans from fungi (1,3:1,6-β-glucans) and β-glucans from barley (*Hordeum vulgare*, Poaceae) (1,3-/1,4-β-glucans). This suggests that the test is less definitive for testing mushroom cultures directly, but arguably very specific for testing blood serum for fungal β-glucans.

Using the Fungitell test, Yang et al. (2003)[106] measured the concentrations of 1,3-β-glucans in a number of species of medicinal fungi and found a wide variation in their percentages. More research is needed to determine the applicability of the Fungitell test for β-glucan quantification in medicinal species of fungi. Although the test is about 10,000 times more sensitive than acid hydrolysis with enzymatic procedures, the Fungitell test is most often used to determine the presence of pathogenic fungi in the blood of immunocompromised individuals. For any utility of the test for medicinal products, the preparation of the sample (such as pretreatments for freeing the β-glucans from chitin linkages) should be carefully optimized.[104]

Using Multiple Tests

Ultimately, the β-glucan content of a particular commercial fungi product, how well it enters into the blood and body tissues, and its potential biological activity should not be determined by assay of the product alone. Rather, multiple tests should be used. For example, a blood serum study, such as the Fungitell test, can be used to determine the level of β-glucans that reaches the blood and circulates to other parts of the body, including the bone marrow[61,107-109]; in vitro studies, as in Coy et al. (2015),[57] can be used to test the immune-stimulating effects of various mushroom extracts; and ex vivo studies (e.g., in which subjects take mushroom products orally and have blood, which contains "primed" immune cells, drawn) can be used to check the cells' ability to resist the damaging effects of free radicals, or to test their killing power in an in vitro system with various pathogens or cancer cells, as in studies published by Tesoriere et al. (2005)[110] and Vanky et al. (1992).[111]

Testing for Other Compounds

Chemical Tests

Chemical tests, such as high-performance thin-layer chromatography (HPTLC), can help ensure products contain a substantial and minimum amount of accepted active compounds, such as β-glucans. At present, the most promising compounds for substantiation of activity in medicinal mushroom products are 1,3-β-glucans, 1,3:1,6-β-glucans, starch/glycogen (1,4- and 1,6-α-glucans), ergosterol, triterpenes, low-molecular-weight compounds like the phenolic hericenones from lion's mane, cordycepin, and others.

Shiitake *Lentinula edodes*. Photo ©2017 Steven Foster

As for triterpenes, these important low-molecular-weight molecules, which have a variety of biological activities, are present in substantial amounts in some species of medicinal mushrooms, such as reishi,[112] and can be identified and quantified by high-performance liquid chromatography (HPLC) or HPTLC methods. The sterol ergosterol is highly specific to fungi, and many studies have been published on methods to quantify the compound, so this marker can be used for determining how much fungal biomass is in medicinal mushroom products.[113] Along with a standard starch/glycogen test, it is possible to determine with fair accuracy how much mycelium or fruiting body, starch, and fillers (e.g., maltodextrin) are in a commercial product. The iodine starch test also can be used, even at home, to detect excessive starch contents in products.

Genetic Analyses

In addition to chemical tests, there are an increasing number of DNA testing options available. For example, with next-generation DNA sequencing (NGS), a mixture of fungal mycelium and substrate can be tested semi-quantitatively for various components. These methods will help ensure the species listed on the label is what is in the product.[114] However, these methods are still under development for the natural products industry.[115-117] According to a recent paper by Raja et al. (2017), researchers were able to use the internal transcribed spacer (ITS), a common DNA marker, to correctly identify a number of fungal species in commercial products.[118]

Additional Quality Control Considerations

Contamination

Another issue regarding products made from mycelia or fruiting bodies is the purity of the source material. When organically grown, mycelia or fruiting bodies from sources in the United States should be free of pesticide residues, heavy metals, and fumigants. When sourced from China or other countries, mushroom products should be checked carefully for proper species identification, purity, and various other quality parameters.

In 2008, $110 million of mushroom products were imported into the United States from China. According to a 2009 US Department of Agriculture (USDA) publication, "Mushroom and fungus products (including dried) were the predominant vegetable type refused" for entry into the United States from 2002 to 2004 and from 2007 to 2008 — in this case, for high levels of pesticide residues.[119] The USDA has also issued import alerts for mushroom products due to contamination with animal filth and insect parts.

In 2004, Singapore and Hong Kong reported heavy metal contamination and unsafe levels of preservatives such as formaldehyde and sulfur dioxide in mushroom imports from China.[120] In addition, in 2014, a government survey in Hong Kong found that cadmium levels were above safe limits.[121] In recent years, however, unsafe levels have not been reported in dried mushroom imports to some Asian countries from China.

Manufacturer Requirements

Considering the possibility of contamination of imported mushroom products, as well as the possibility of fumigation when entering the United States, companies should carefully test each batch for proper identity and potential levels of contaminants. USDA regulations state that dried mushrooms can enter the United States when they are free of soil, insects, diseases, and contamination.[122]

For dietary supplements sold in the United States, numerous tests are available to manufacturers to ensure their products are free of contamination of any kind, excessive amounts of filler, or undigested substrate in the case of grain-grown mycelial products. It is the responsibility of the manufacturer to perform these frequently on all ingredients, especially when suppliers or batches change and even if the manufacturer has received a certificate of analysis (COA) with the ingredient from a supplier. (Inaccurate and/or falsified COAs from ingredient vendors have been reported in the general botanical and conventional food trade. Buyers should contact the manufacturer and ask questions about their purity, activity, and identity testing program.)

Product Labeling

The part of the fungi (mycelium or fruiting body) included in a commercial product should also be clearly labeled, especially on the ingredients panel. The American Herbal Products Association, a national trade association for the botanical products industry, has hosted discussions with medicinal mushroom manufacturers about whether it is misleading to consumers to use the term "mushrooms" on products that contain 100% mycelium grown on rice or other grains. As a general term, "medicinal mushrooms" on the front panel might alert consumers who may not be familiar with the term "medicinal mycelium." On the other hand, the use of "mushrooms" on the ingredients panel when the product contains 100% mycelium with some (or even a substantial amount of) residual cooked grain would be misleading, according to some industry experts. As discussed previously, mushroom fruiting bodies and mycelia both offer health benefits, but they are not necessarily equivalent.

Conclusion

While assays for β-glucans, ergosterol, starch, and specific low-molecular-weight compounds in finished products are useful as a starting point, multiple additional assays (e.g., blood serum studies and bioassays to assess immune activation and absorption of glucans or other compounds) are warranted to guarantee the quality and efficacy of medicinal mushroom products.[57]

The issue of whether mycelium- or fruiting body-derived products are more active is worth consideration, but many other factors play a role in the chemistry and biological activity of finished products. Such factors include, but are not limited to, the species, genotype, and strain of the organism; the substrate, nutrient availability during growth, atmospheric conditions, and other

Reishi *Ganoderma lucidum*
Photo ©2017 Steven Foster

Maitake *Grifola frondosa*
Photo ©2017 Steven Foster

Turkey tail *Trametes versicolor.* Photo ©2017 Chris Hobbs

Whitish truffle *Tuber borchii.* Photo ©2017 Mortazavifar (WikiCommons)

Cordyceps militaris. Photo ©2017 Andreas Kunze (WikiCommons)

environmental factors; as well as the time of harvest in the growth cycle and methods of drying, extraction, and product manufacturing. Additional controlled clinical studies are needed to sort out these important issues in order to maximize the effectiveness of fungal-derived preparations and products. HG

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Author Chris Hobbs with turkey tail (*Trametes versicolor*).

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NASC Preferred Supplier Program Focuses on Quality Standards in Animal Supplement Industry

The National Animal Supplement Council (NASC) is a California-based nonprofit industry advocacy and educational group that is dedicated to protecting and enhancing the health of companion animals (dogs, cats, and horses) in the United States.

Founded in 2002, the NASC is made up of more than 140 businesses that are committed to providing high-quality health supplements and nutritional supplements for these animals. Health supplements, such as those that contain glucosamine, chondroitin sulfate, methylsulfonylmethane (MSM), parsley (*Petroselinum crispum*, Apiaceae), and peppermint (*Mentha* × *piperita*, Lamiaceae), are intended to support maintenance of normal biological structures and functions. Nutritional supplements, such as those that contain vitamins and minerals, are intended to provide nutritional value as a component of a complete and balanced diet.[1,2]

NASC members are located around the world, including in the United States, Canada, Europe, Australia, and China. An NASC Primary Supplier Member must be a manufacturer, formulator, bottler, labeler, or re-packer that markets its brand as the supplier of record. An NASC Associate Member may be involved in selling or distributing animal health/nutritional supplements as a distributor, dealer, retailer, veterinarian, or internet/catalog company.

All NASC members are vetted in a direct interview that presents and clarifies the requirements of the organization and the standards to uphold. In addition, most NASC members complete an independent NASC quality audit that, when passed, enables them to display the yellow NASC Quality Seal on their packaging and marketing materials. NASC membership demonstrates a commitment to upholding specific quality standards, which the NASC hopes, in turn, will increase consumer confidence in the animal supplement industry.[2]

Preferred Supplier Program Overview

The NASC Preferred Supplier Program is a self-regulatory program that was initiated to help extend responsibility, accountability, and uniformity upstream to the beginning of the animal supplement supply chain. It also helps NASC members identify reputable suppliers of reliable raw materials. "With the increased scrutiny on suppliers and supply chain management, our intention has been, always, to keep our members ahead of the regulatory curve," said Bill Bookout, president of the NASC and chair of its board of directors (oral communication, August 31, 2016).

The NASC's Preferred Supplier Program helps all parties involved save time and money through data sharing. Suppliers avoid having to submit to audits for every customer, and NASC members do not have to go through the process of qualifying each supplier. Thus, all parties contribute to the program and all parties benefit from the program, according to Bookout.

The program qualifies suppliers in four categories: Raw Material Suppliers, Contract Manufacturers (many NASC member companies that market their own brand of products rely on one or more third-party manufacturers to produce their products), Laboratories and Research, and Service Providers (e.g., insurance providers, packagers or providers of packaging components, legal service providers, web service providers, etc.). So, in the context of the NASC's program, the term "Preferred Supplier" encompasses a wide variety of product and service providers along the supply chain and is not limited only to suppliers of raw materials.[3]

Peppermint *Mentha* × *piperita*
Photo ©2017 Steven Foster

Each company in the Preferred Supplier Program pays an annual fee, which covers the posting of all Preferred Supplier information in the "Members" section of the NASC's website, the posting of a company sales profile for all Preferred Suppliers, the opportunity to conduct webinars and/or educational programs for NASC members, the availability of contacts at NASC member companies, attendance at the Preferred Suppliers Only Meeting during the NASC Annual Conference, and the opportunity to provide input about the program.

Raw Material Suppliers and Contract Manufacturers must complete and submit a Preferred Supplier Data Sheet, which includes information about the manufacturing facility, testing information, current good manufacturing practice (cGMP) compliance details, and more. In addition, Raw Material Suppliers must complete and submit a Non-Botanical Ingredient Data Sheet or a Botanical Ingredient Data Sheet for each unique ingredient that the company supplies.

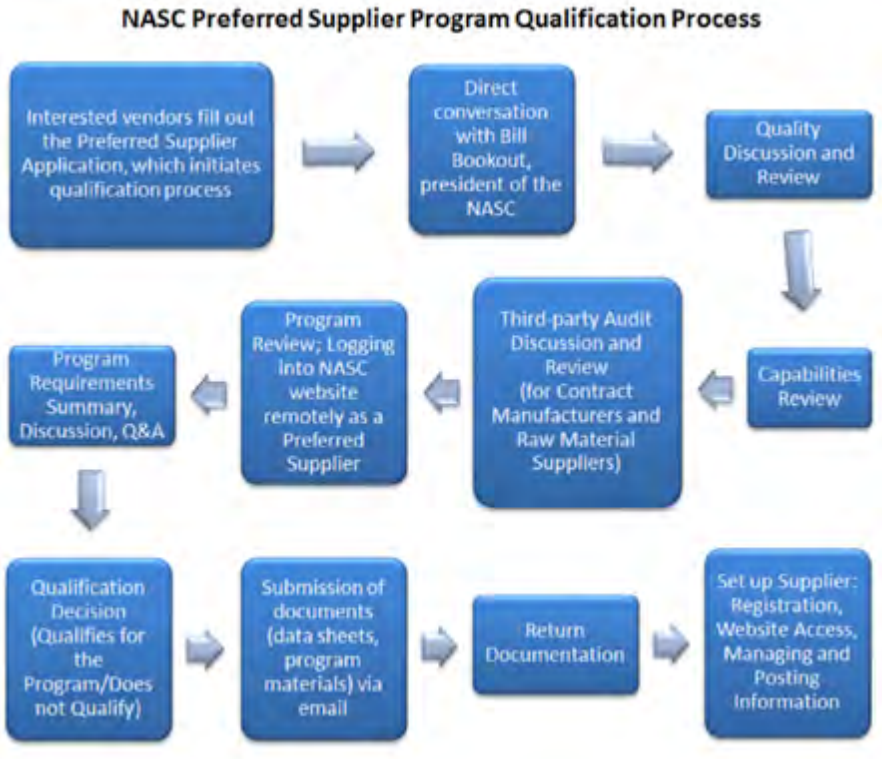
These data sheets are modeled after the data sheets of the Standardized Information on Dietary Ingredients (SIDI) protocol, but have been adapted for the animal supplement industry. The SIDI initiative is a voluntary, industry-wide protocol intended to standardize and streamline communication of information about dietary ingredients from raw material suppliers to finished product manufacturers. It is a cooperative effort among three of the leading trade associations for the dietary supplement industry: the Consumer Healthcare Products Association (CHPA), the Council for Responsible Nutrition (CRN), and the United Natural Products Alliance (UNPA).[4]

For each ingredient that is qualified by the NASC's program, samples from five batch/lot numbers (from one supplier) of that ingredient must be tested to verify the information on the respective certificate of analysis (COA) that accompanies each batch/lot. A COA is the supplier's test results for the batch/lot of raw material being supplied. The information provided on the COA depends on the raw material, but it usually includes information about quality, strength, purity, and composition. It may also include notation of the plant part(s) used (for botanical ingredients), the geographical source of the raw material, concentrations of marker compounds, and levels of potential contaminants (if detected), including microbial (e.g., *Salmonella* and *Escherichia coli*) count and heavy metal (e.g., lead, mercury, cadmium, and arsenic) count. In the case of boswellia (*Boswellia* spp., Burseraceae), for example, the COA could include boswellic acid content. For garlic (*Allium sativum*, Amaryllidaceae), it could include allicin yield. Methods of analysis are also noted.

Samples from the first two batch/lot numbers may be tested by the Raw Material Supplier from their own in-house laboratory or submitted by the Raw Material Supplier for testing by an NASC-approved laboratory. However, samples from the other three batch/lot numbers must be submitted either by an NASC member that sources the ingredient from that supplier, or by another customer of that supplier that uses the ingredient in its product formulations, for testing by an independent, third-party, NASC-approved analytical laboratory in the United States. The three independent tests, which are conducted at the expense of the supplier, break the chain of custody and eliminate sample bias. These tests may be performed by the laboratories that are listed as Preferred Suppliers on the NASC's website or by other reputable laboratories in the industry.

All raw materials must be tested using methodology that follows current established recommendations of the United States Pharmacopeia (USP), AOAC International, other recognized testing authorities, published monographs (including monographs of the American Herbal Pharmacopoeia [AHP]), or other published testing methods. Each raw material qualified by the NASC's program is subject to re-verification with one random test performed annually.

Raw Material Suppliers must meet these requirements for each individual ingredient in order for those ingredients to be qualified by the NASC's program, but there is no additional fee for qualifying additional ingredients.



For Contract Manufacturers and Raw Material Suppliers, the NASC will recognize facility audits that have been conducted by NSF International, the Safe Quality Food (SQF) Institute, Underwriters Laboratories (UL), the Natural Products Association (NPA), and other auditing bodies that are accredited to confirm that manufacturing facilities are operating in accordance with dietary supplement cGMPs, as described in 21 CFR (Code of Federal Regulations) Part 111. This regulation requires "persons who manufacture, package, label, or hold a dietary supplement to establish and follow current good manufacturing practice[s] to ensure the quality of the dietary supplement and to ensure that the dietary supplement is packaged and labeled as specified in the master manufacturing record."[5]

The NASC requires Contract Manufacturers and Raw Material Suppliers to have a current audit certificate. Typically, these certificates expire every one or two years. If a Contract Manufacturer or Raw Material Supplier has not been audited, the NASC can conduct a facility audit, but this takes more time.

Laboratories seeking qualification by the NASC's program must complete and submit an Analytical Laboratory Data Sheet. These laboratories must comply with good laboratory practices (GLPs) and good analytical methodology (as recommended by the USP, AOAC International, etc.). In addition, Service Providers must complete and submit a Service Provider Data Sheet.

The data sheets submitted by all of the Preferred Suppliers, along with the required testing information and any additional documentation (e.g., kosher statement, hormone statement, sterilization methods [irradiation, ethylene oxide] statement, genetically modified organism statement, and

Table 1: Top-Selling Pet Supplements Overall

Primary Ingredient	Sales	% Change from Previous Year
Glucosamine	$21,244,413	-6.1%
Glucosamine/Chondroitin Combination	$20,513,548	57.3%
Vitamin E (Not Ester-E)	$6,998,649	108.6%
Multiple Vitamin (Adult)	$4,630,069	-7.5%
Animal Protein (Whey and Casein)	$3,934,666	127.0%
Parsley (*Petroselinum crispum*, Apiaceae)	$2,794,133	-12.9%
Zinc	$2,754,218	214.1%
Animal and Plant Protein Combination	$2,544,139	19.5%
Chlorophyll/Chlorella	$2,039,035	-62.3%

Source: SPINS / Cross-channel aggregate* for the 52-week period ending November 27, 2016

Table 2: Top-Selling Herbal Pet Supplements

Primary Ingredient	Sales	% Change from Previous Year
Parsley (*Petroselinum crispum*, Apiaceae)	$2,794,133	-12.9%
Chlorophyll/Chlorella	$2,039,035	-62.3%
Peppermint (*Mentha* × *piperita*, Lamiaceae) and Other Mints	$1,831,908	38.2%
Pumpkin (*Cucurbita pepo*, Cucurbitaceae)	$862,966	150.4%
Chamomile (*Matricaria recutita*, Asteraceae)	$465,978	-32.6%
Flax (*Linum usitatissimum*, Linaceae) Seed and/or Oil	$249,602	7.9%
Menthol (Derived from *Mentha* species)	$173,344	-11.0%
Lavender (*Lavandula angustifolia*, Lamiaceae)	$143,232	-0.4%
Garlic (*Allium sativum*, Amaryllidaceae)	$124,020	-73.2%
Tea Tree (*Melaleuca alternifolia*, Myrtaceae) Oil	$113,826	34.2%

Source: SPINS / Cross-channel aggregate* for the 52-week period ending November 27, 2016

organic certification statement, etc.) are available for NASC members to download on the NASC website. In addition, Preferred Suppliers may also choose to post liability insurance certificates.

Preferred Suppliers, however, are not required to post confidential information, such as proprietary processes or anything covered under trade secrets. Preferred Suppliers may choose to make certain information available to the NASC under a non-disclosure agreement (NDA). Additionally, distributors are not required to disclose their suppliers, since manufacturers could then cut them out and go directly to the supplier, but distributors must be able to verify how their suppliers were qualified.

Ingredients that have been qualified by the program are searchable by common name on the NASC website. Each common name listing includes all of the Raw Material Suppliers that have been qualified to supply that particular ingredient, in addition to the required testing information and additional documentation.

Chamomile *Matricaria recutita*
Photo ©2017 Steven Foster

Conclusion

Currently, more than 60 Preferred Suppliers, some of which are also NASC members and most of which are located in the United States, have been qualified by the NASC's program. These Preferred Suppliers are able to display the blue NASC Preferred Supplier Seal. "Our goal with the program is not to get every single company that possibly participates in this industry into the program," said Bookout (oral communication, December 15, 2016). "Our goal is to get quality suppliers into the program, to differentiate them from opportunistic suppliers, and to reduce the ever-increasing cost of quality and qualifying suppliers."

According to Bookout, the NASC's program has qualified most of the main ingredients commonly used in animal supplements (Table 1), such as glucosamine and chondroitin,† MSM,‡ and hyaluronic acid.** However, the NASC hopes to start qualifying more herbal ingredients (Table 2) under the program soon. According to data from the Chicago-based market research firm SPINS, cross-channel aggregate sales of animal supplements totaled almost $110 million in the 52-week period that ended November 27, 2016, an 11.2% increase in sales from the previous year.

The Preferred Supplier Program officially began in 2014 and, in 2016, it grew significantly, according to Bookout. He also said that the feedback the NASC has received about the program has all been extremely positive.

* Includes sales in the Natural Channel, Specialty Gourmet Channel, and Conventional Channel. The SPINSscan Natural Channel includes products sold at full-format natural product supermarkets, small to mid-sized chains, and independent and cooperative stores across the continental United States (excluding sales at Whole Foods Market). The Specialty Gourmet Channel includes products sold at full-format supermarkets with more than $2 million in annual sales, with SPINS-defined specialty items making up at least 25% of their overall volume. The Conventional Channel includes natural, organic, specialty, and wellness products sold at conventional outlets in the United States (data determined in collaboration with Information Resources Inc. [IRI Worldwide]).

† Glucosamine and chondroitin are compounds derived from cartilage and are often used in combination to treat conditions associated with osteoarthritis.[6]

‡ MSM is a natural compound found in some primitive plants (e.g., *Equisetum arvense*, Equisetaceae) and other natural sources, and that can be prepared through oxidation of dimethyl sulfoxide. It is used to treat a variety of conditions, such as arthritis, joint inflammation, tendonitis, and musculoskeletal pain.[7]

** Hyaluronic acid is a compound found in the tissues and body fluids of vertebrates, and in some bacteria, that can help with joint lubrication, water homeostasis, filtering effects, and regulation of plasma protein distribution.[8]

Bookout said the NASC is also planning to expand the program beyond dietary supplements for animals. "We are going to expand the program out to pet food and pet treats manufacturers as well," he said.

The NASC's Preferred Supplier Program was put together with the help of NSF International auditors. "I have been told by everyone who has looked at it that it will stand up to the independent scrutiny of a third-party audit," said Bookout. "At the end of the day, consumer confidence is increased, and, in our case, the animals benefit." HG

—Connor Yearsley

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Animal Supplement Industry Regulation in the United States

The NASC was established to provide a complete regulatory and compliance pathway for the animal supplement industry because of the absence of a legal category for animal dietary supplements and because of apparent efforts by regulatory bodies to remove many of these products from the market.[9]

In 1994, the Dietary Supplement Health and Education Act (DSHEA) was passed, and it classified dietary supplements as a category of food under the Federal Food, Drug, and Cosmetic Act. This meant that dietary ingredients could be used without premarket approval as long as they were marketed in dietary supplements before October 15, 1994.[9-11] However, DSHEA did not address animal supplements, probably because that segment was very small at the time and because the purpose of the legislation was to address the increasing demand for human dietary supplements,[9] as well as consumer and industry concerns at the time about government regulations that would have limited access to many supplements.

In 1996, the Food and Drug Administration's (FDA's) Center for Veterinary Medicine (CVM), which is primarily responsible for the regulation of animal food and drugs, stated that DSHEA does not apply to animal products, reasoning that ingredients with a history of safe use in human dietary supplements may not necessarily be safe for animals. Different animal species require different nutrients, absorb and metabolize substances differently, and may exhibit different toxic reactions to substances.[10]

Therefore, products marketed as animal dietary supplements, which typically fall under the category of "animal feed," are still subject to the pre-DSHEA regulatory environment and usually must be made up of ingredients that are generally recognized as safe (GRAS), approved as food additives, or listed in the *Official Publication of the Association of American Feed Control Officials*.[11]

Animal supplement claims are limited to those pertaining to the nutrition, taste, and/or aroma of the product. In some cases, the CVM allows claims of "nutritional support" of specific organs and/or body functions. As with human dietary supplements, animal supplements that claim to treat, mitigate, or prevent disease are considered unapproved new drugs.[11]

The Food Safety Modernization Act (FSMA), which was passed in 2011 and emphasizes preventing contamination in the food chain instead of responding to it, established cGMPs for animal food production. So, animal supplements marketed as food are subject to FSMA rules.[12]

What Have Plants Ever Done for Us? Western Civilization in Fifty Plants by Stephen Harris. Oxford, UK: Bodleian Library, University of Oxford; 2016. Hardcover, 264 pages. ISBN: 978-1851244478. $25.00.

Stephen Harris is the Druce Curator of the Oxford University Herbaria and a university research lecturer. In this book, he has written an excellent and lively set of fifty essays, deftly and artistically weaving scholarly research with ancient and modern botanical history. Contributing new information on old plants is a feat in itself, and Harris has managed to do so in an inviting, conversational style. His objective is to show a wide range of potential readers that plants matter to all life forms, even in the most modern urban settings.

The point of view is Western, as indicated in the subtitle. Harris cites the Egyptian Ebers Papyrus, not the Chinese Pen Ts'ao or documents from Indian Ayurveda, though the narrative ranges globally in the story of ethnobotany. In an impressively slim volume, Harris covers five major arenas in which plants have had indispensable effects on humans: in history and trade, as food, in the politics of empires, as medicine, and in industry. As one who studies history as well as herbal medicine, I expected some of the "mainstage players," as Harris describes them in his table of contents. Some choices will be well known to many readers, such as wheat (*Triticum aestivum*, Poaceae), sugar (*Saccharum officinarum*, Poaceae), coffee (*Coffea arabica*, Rubiaceae), tea (*Camellia sinensis*, Theaceae), corn (*Zea mays*, Poaceae), and rice (*Oryza sativa*, Poaceae). What grabbed my attention was how odd other choices seemed at first: "Thale cress?" I wondered. It was a pleasure to discover why his 50 favorites made the cut.

Harris begins with an introduction suitable for his intended wide audience, many of whom may not be familiar with the ways plants have influenced the way we live. There is a brief, yet accessible, introduction to how plants are studied and how their names reveal much. He draws the reader into a cozy chat about broad swaths of human uses of plants. The introduction is followed by profiles ranging from barley (*Hordeum vulgare*, Poaceae) to, yes, thale cress (*Arabidopsis thaliana*, Brassicaceae). These fifty chapters, each three pages or so, will deepen readers' understanding of ethnobotany, but Harris is not always focused on medicinal uses. This is not another herbal or how-to book.

Each chapter opens with the common name, scientific nomenclature, family, and a fine black-and-white line drawing. The plant profiles are supported by extensive references, 491 in all, ranging from John Gerard's 1597 *Herball* and earlier, with many 18th, 19th, and 20th century treatises, letters, and texts, through to an abundance of research from 2000 to 2014.

The story of coffee begins with the legend of its discovery by goatherds, though not the often-cited first use in Coptic monasteries. Harris explains how the Dutch traded the island of Manhattan for nutmeg (*Myristica fragrans*, Myristicaceae) and other commodities, but he does not mention nutmeg's medicinal applications. The book also features graphical depictions of evocative quotes. For example, a quote in the chili (*Capsicum* spp., Solanaceae) section reads: "chemical pain has become organoleptic pleasure." The discussion of its constituent capsaicin offers good historical information from the Americas, yet Harris omits chili's use for pain and as a styptic (i.e., a type of antihemorrhagic). Having previously published on grasses, Harris brings his passion for them to the page in several chapters. He writes of the way meadow grass (*Poa pratensis*, Poaceae) changed the evolution of Europe over 5,000 years, exemplifying the crux of our dilemma between feeding increased populations while losing biodiversity.

A brief section titled "Further Reading" includes gems such as *Seeds of Change* (H. Hobhouse, 1999), *Guns, Germs and Steel* (J. Diamond, 1998), and *The Thief at the End of the World: Rubber, Power, and the Seeds of Empire* (J. Jackson, 2008). The reading list alone is an intriguing window into the way humans view plants, from Queen Elizabeth I to those involved in contemporary debates over biofuel. The index that completes the book manages to be both concise and comprehensive, considering the range Harris successfully covers.

As a clinician who uses medicinal plants, I appreciate Harris's scientific precision, but I would have liked more information about the plants' health-related properties. For example, the chapter on grape (*Vitis vinifera*, Vitaceae) focuses on wine rather than resveratrol, a widely studied chemical component of wine. Discussion about the current trend toward medicinal applications of cannabis (*Cannabis* spp., Cannabaceae) is absent, though Harris presents information on its ritual use and the importance the plant fiber had for navies. Entries in which the medicinal use was one of the chapter's primary emphases include opium poppy (*Papaver somniferum*, Papaveraceae), Pacific yew (*Taxus brevifolia*, Taxaceae; which produces the anticancer compound taxol), and species of the genus *Cinchona* (Rubiaceae). The bark of some *Cinchona* species is the original source of the antimalarial compound quinine. This chapter is a good example of why this book is such a fine addition to botanical libraries; rather than recounting the familiar stories regarding "Jesuit's Bark" (the genus of which was named after the Condesa de Chinchón), Harris offers a highly entertaining anecdote about a possible link to Oliver

Cromwell's death from malaria (Hint: Cromwell had a hostility to anything Catholic). There are also discussions about the players who were determined to obtain quinine for over two centuries, who profited from trade secrets, often illegally, and who murdered indigenous *Cinchona* experts (allegedly the Bolivian government).

Eight of the 50 plants examined include some reference to genetic engineering. In the chapter on the "democratization" of pineapple (*Ananas comosus*, Bromeliaceae), Harris describes how the selective breeding of the fruit to fit in cans transformed it from a food for royals and the wealthy to a food available to all. Harris seems in favor of genetic technologies, though he notes some concerns in relation to food production. Regarding tomatoes (*Solanum lycopersicum*, Solanaceae), Harris notes that "the potential health benefits of genetically modified plants may yet sway public opinion." For many herbal scientists, this will spark controversy. This seems part of the intention of the book: to generate discussion among the learned and all those dependent on plants — that is to say, everyone.

Harris has taken 50 important plants, diving deep and wide into both ancient and the most current human stories with a light touch. This allows certain facts of inhumanity presented here to speak for themselves: Britain's ignoble Opium Wars with China, slavery and other human rights abuses, environmental disasters, and the 1988 murder of Amazonian rubber tapper and conservationist Chico Mendes.

In *What Have Plants Ever Done for Us?*, Harris aims to share big ideas with people from all walks of life. This book is a pleasure cruise of plant science, and it will be of interest to anyone interested in the planet, from secondary school biology students to educators and health care professionals. Rich in research details, this is a unique resource for any reader who teaches, gives public talks, or seeks to update academic lectures on botanical topics. Harris has achieved a mighty goal in shining a bright light on our debt to and dependence on plants, from grass to towering tree. HG

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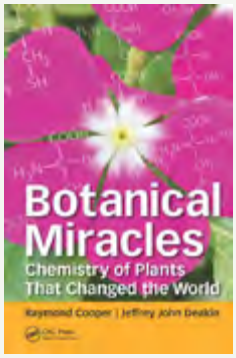
Botanical Miracles: Chemistry of Plants that Changed the World by Raymond Cooper and Jeffrey John Deakin. Boca Raton, FL: CRC Press; 2016. Hardcover, 252 pages. ISBN: 978-1-4987-0428-1. $119.95.



The authors state that the purpose of this book is to "supplement and extend the teaching curriculum by providing context for learning in organic chemistry ... [and] to inspire, enhance and enrich an inquiring mind through a multidisciplinary approach; embracing science, medicine, the natural environment, geography and history." The text is presented as a series of case studies of individual natural molecules that are organized by various categories, such as medicines, foods, beverages, euphorics (natural drugs with abuse potential), cosmetics, and colorants.

Within each individual case study is an exploration of the molecule's main functional group(s) and how the basic chemical structure of the molecule corresponds to various functions or characteristics. Some generalized synthetic organic chemistry schemes are presented with respect to the functional groups found in the highlighted molecule, along with some discussion on the isolation/production of the molecule from natural and/or synthetic sources. The history of use and societal context and impact (e.g., regulation, social aspects, environmental consequences, etc.) are included. Additional discussion may be offered on other molecules of the same structural class or on synthetic substitutes for the highlighted natural molecule(s).

In some cases, there is discussion on various analytical techniques, such as spectroscopy (e.g., nuclear magnetic resonance [NMR]) and chromatography, which can be found readily in any organic chemistry textbook. The authors wanted to be very comprehensive, but the book might have been strengthened by focusing a bit more on the unique perspectives the authors could bring to bear on the selected natural molecules. In some sections, the book is weakened by the inclusion of information that is only peripherally related to the initial molecule of focus. For example, the section on "A Steroid in Your Garden" includes a discussion of vitamin C and other vitamins that are not steroids.

In the section that includes taxol, a chemotherapy drug isolated from the bark of the Pacific yew (*Taxus brevifolia*, Taxaceae), a discussion about stereochemistry (i.e., the study of the spatial arrangement of atoms and molecules) and chirality might have logically wrapped back around to mention the numerous stereocenters of the featured molecule and their implications in regards to the molecule's synthesis, but this was not done. From this perspective, although the authors appear to have fulfilled the purpose of the book, some streamlining for a future edition could also be envisioned.

There are some minor factual errors that it would be useful to correct if there are plans for a second edition, such as proper credit to Monroe Wall, PhD, and Mansukh Wani,

PhD, as the co-discoverers of taxol (not "Monroe and Wall," as stated), as well as the substitution of a photo of coffee (*Coffea arabica*, Rubiaceae) beans for what should have been cocoa (*Theobroma cacao*, Malvaceae) beans in Figure 4.3. In the latter case, even the cited photo source misidentified the beans. Some of the images used as figures do not have a credit or copyright designation.

There are some places where the authors' definitions deviate from mainstream chemical concepts. An example: "Lipids, also known as fatty acids…." Fatty acids are, rather, one type of lipid, whereas lipids also include molecules such as aliphatics, sterols, triglycerides, waxes, oils, etc. Another example: "An essential oil is an *aqueous* [emphasis mine] mixture containing the volatile hydrophobic compounds of an individual plant…." Essential oils are mixtures of volatile, hydrophobic compounds, not aqueous compounds. Rather, a *hydrosol* is the steam distillate of a plant that has mainly aqueous content and some tiny amount of volatile oils (which also may be present in the essential oil fraction), so perhaps the insertion of the word "aqueous" was inadvertent.

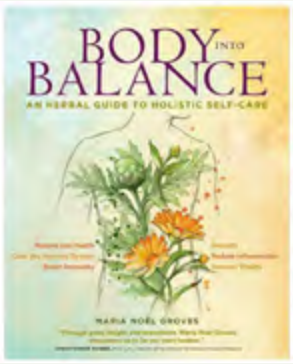
The above items notwithstanding, this book is still a unique contribution to the reading list of the undergraduate or graduate organic chemistry educator who wishes to provide his or her students with a stimulating collection of information, both scientific and anecdotal, about some of the most influential natural products worldwide.

The book is not necessarily a reference guide, but rather, a unique textbook that would, in my opinion, be well-intended for use by advanced organic chemistry students. I would not recommend the content to anyone who has not yet taken an organic chemistry class, since I think it would be too advanced. However, it would be appropriately used as part of an advanced organic chemistry or natural products class. The questions at the end of each case study are useful for stimulating additional discussion and could even be used as inspiration for independent projects when appropriate for the curriculum.

A bit eclectic and possibly wandering in some areas (as many good stories are), the fundamental chemistry of natural products that have had a significant social, economic, or medical impact on the world is covered well overall. I especially appreciate the historical anecdotes that provide the "story behind the molecule" in some cases. *Botanical Miracles* is a good read, and I recommend it for undergraduate and graduate organic and/or natural products chemistry students and educators. HG

—Nancy L. Booth, PhD
Bethesda, Maryland

Body into Balance: An Herbal Guide to Holistic Self-Care by Maria Noël Groves. North Adams, MA: Storey Publishing, LLC; 2016. Softcover, 336 pages. ISBN: 9781612125350. $24.95.



Readers today live in an era of self-care. Many individuals are looking beyond conventional systems of medicine for answers, and numerous options for self-experimentation, empowerment, and information are available online and elsewhere. The internet brims with ideas and thoughts on using plants for self-care, although there is little consistency in the quality of the information.

The practice of herbal medicine has roots in self-guided care. Samuel Thomson's *New Guide to Health, or Botanic Family Physician*, published in 1822, guided the average farmer and homesteader to be their own herbalist, and a plethora of unpublished herbal traditions describing treatments and medicines have been passed down through oral tradition. Today, many individuals are removed from bioregionally bountiful medicinal plants and the tradition of herbal medicine as continuous self-care, which has left some hungry for the cultural knowledge of the past.

Body into Balance steps into this role with grace. Full of images that depict plants and herbal practices, it evokes the spirit of the early self-care texts and adds a modern spin. Author Maria Noël Groves systematically addresses modern health concerns and presents dietary, lifestyle, and herbal self-care recommendations for health-conscious individuals.

After introducing the "Foundations of Good Health," which offers details of basic wellness care, Groves explores the common functional aspects of the body, providing fundamental information on maintaining health, as well as herbal medicines that may be employed for common conditions. Many of the sections are delightful, such as "The Respiratory System: Breathing Deeply," in which Groves elaborates on how an herbalist might view the maintenance and support of this dynamic system through a look at different imbalances and herbal approaches to correcting such dysfunctions. This section also contains a useful chart displaying a detailed materia medica for the respiratory system as a reference tool.

Beyond the sections on health and disease, there are recipes and explanations of complementary therapies, and an attractive and useful section dedicated to medicine-making that provides the instructions and details needed to begin a foray into self-care practices.

At times, the text comes dangerously close to making a number of medical pronouncements without the typical provision of evidence to support them. There is a very fine

line today between folkloric and empirical understanding of herbal actions, and the evidence base and mechanisms of action that reinforce them, and this book struggles at times with that distinction. How can a text targeted to a non-medical audience offer self-care for complicated medical conditions without sounding too technical and prescriptive? Is it appropriate to suggest self-care for complicated medical conditions? How can we explain how an herb actually works in the body in a general way without being inaccurate or overly simplistic?

Given the safety and overwhelming, common-sense benefits of the herbal therapies discussed, Groves's recommendations put trust in the consumer to navigate their own health care choices. But it is far from a shot-in-the-dark approach: The content here is a product of extensive training and clinical experience.

Trust in the individual is a recurring theme in this book, as when Groves discusses support for people with cancer, irritable bowel syndrome, and other serious conditions. Always careful to remind readers that these conditions are not to be self-treated, she proceeds to provide information for readers to make their own choices about the botanical aspects of their care. While patients may be delighted by this clinical-based information, the recommendation to seek out the care of a trusted and skilled herbal medicine professional could have been made more frequently. This would have better enforced the fact that while self-care is a pillar of health, there are limitations to the practice, and professionals who specialize in herbal therapies are available for support.

There is a distinct dichotomy of herbal health care books today: Some focus on the professional and are thick with terminology and references, and others are directed toward the "lay person" and consist of general language and are tradition-oriented. This book ventures into a bit of unknown territory and is a bold guide meant for all. It lays down the simple principles of how an herbalist would evaluate and support the individual. Despite the discomfort of those who may prefer a distinction between the standards for medical literature and for works prepared for general consumption, this book may be just what the ever-hungry body of patients, searching the internet for answers, needs at the moment. HG

—Bevin Clare, RH, CNS
Associate Professor,
Master's of Science in Herbal Medicine,
Maryland University of Integrative Health;
President, American Herbalists Guild
Laurel, Maryland

Medicinal Plants and Malaria: Applications, Trends, and Prospects by Woon-Chien Teng, Ho Han Kiat, Rossarin Suwanarusk, and Hwee-Ling Koh. Boca Raton, FL: CRC Press; 2016. Hardcover, 472 pages. ISBN: 9781498744676. $89.95.

Malaria remains one of the most persistent and pressing global public health problems of our time, despite decades of eradication and control efforts. It is one of the deadliest vector-borne diseases, killing more people today than it did 40 years ago, and it affects millions worldwide, especially in sub-Saharan Africa and Southeast Asia. The endemic poverty associated with the malaria burden and the magnitude of its effects call for an action paradigm that links traditional treatment approaches to modern technology, while addressing the nexus of environmental, economic, and political dimensions that sustains this deadly disease. The use of medicinal plants and their constituents to combat malaria offers a broad-spectrum approach that meaningfully addresses both the proximal and fundamental causes of malaria. *Medicinal Plants and Malaria: Applications, Trends, and Prospects* provides a review of plants used traditionally in the treatment of malaria, includes a tabular summary of candidate antiplasmodial compounds, and highlights selected medicinal plants that have been evaluated clinically for the treatment of the disease.

The authors adopted a tabular approach, which enabled them to summarize enormous amounts of data in fewer pages than it would have taken to present such information otherwise. The tables feature comprehensive lists of plant species used for treatment and/or prevention of malaria worldwide, with details on plant parts used, methods of preparation, and clinical reports where available. The tables also collate useful information on malaria, current prevention and treatment strategies, and scientific research carried out on some of the plant species, including several ongoing studies.

Chapter 1 gives a brief introduction of malaria epidemiology, the global public health implications of the disease, the life cycle of *Plasmodium* parasites, and the clinical presentation of the disease. It describes a disease that is endemic in 104 countries and a risk to 3.4 billion people, mainly in the tropical parts of the world. It is estimated that, in 2012, 207 million malaria cases occurred globally, killing approximately 627,000 individuals. About 80% of these cases and 90% of the deaths occurred in Africa. Most of the deaths (77%) were children younger than five years old.

Chapter 2 discusses currently available antimalarial drugs, and their modes of action and roles in clinical

therapy, including possible combinations with other drugs to enhance their therapeutic value. This is followed by a table of country-specific recommendations for malaria prevention. This information, which was adapted from credible sources such as the World Health Organization (WHO), the US Centers for Disease Control and Prevention (CDC), and the UK-based Public Health England, will be of immense value to clinicians and those interested in travel medicine.

Chapter 3 contains a review of published literature on medicinal plants used for malaria, including those that are currently in clinical use in various countries. It discusses the latest findings from ethnobotanical research, the outcomes of bioassay-guided isolation of antiplasmodial phytochemicals from medicinal plants, and results from clinical trials and public health interventions using medicinal plants.

Chapter 4 is about clinically important medicinal plants, with understandable focus on *Cinchona* (*Cinchona* spp., Rubiaceae) bark, *Artemisia annua* (Asteraceae), *Dichroa febrifuga* (Hydrangeaceae), and *Vernonia amygdalina* (Asteraceae). The chapter also contains profiles of four popular herbal formulations used in experimental malaria therapy: Sumafoura Tiemoko Bengaly (Mali), N'Dribala (Burkina Faso), Phyto-laria (Ghana), and PR 259 CT1 (DR Congo). Rather than focusing on the African proprietary formulations, the chapter should have focused more on the published information and in-depth analyses available for the plant species (*Argemone mexicana*, Papaveraceae; *Cochlospermum planchonii*, Bixaceae; *Cryptolepis sanguinolenta*, Apocynaceae; and *Nauclea pobeguinii*, Rubiaceae). Given the high mortality of the disease in Africa, as reported in Chapter 1, any effective home-grown remedy would likely significantly reduce the malaria burden on the continent and perhaps also minimize the associated economic effect.

Chapter 5, the final section of the volume, contains a summary of the preceding chapters and a general discussion about malaria control and treatment. Of particular interest is the suggestion for the use of cocktail therapy in clinical malaria treatment, which has been successfully applied in the treatment of tuberculosis, HIV/AIDS, and cancer.

A major problem highlighted in the book is the rather poor rate of translation of results from laboratory studies on medicinal plants into therapeutic agents. Although phytochemical and phytopharmacological studies of natural remedies have yielded a rich bounty of important therapeutic agents (used either as single-chemical entities or as mixtures of chemically defined molecules in phytomedicines), the ratio of identified bioactive entities (molecules and mixtures) that have shown activity in vitro and/or in vivo and subsequently were found to be active in clinical studies is rather low (2,000,000:1).

Clinical translation of laboratory studies also has been slow due to the lack of ideal and established solutions for precise targeting, cell internalization, and controlled drug solubility and release of the active compounds. The book encourages the use of standardized herbal preparations rather than isolated pure compounds in malaria therapy and drug development since this corresponds with the method of use in many traditional medicine systems. The rest of the book consists of an appendix (pages 139-415) that lists antimalarial plants, and a well-annotated index.

This book will serve as an excellent reference volume for students, teachers, health care professionals, and researchers interested in medicinal plants and promising antimalarial preparations. It will appeal to a diverse audience, including pharmacognosists, phytochemists, pharmacologists, pharmacists, herbalists, physicians, and naturopaths, as well as scientists engaged in research in natural products, drug discovery, biodiversity, medicinal chemistry, and other related fields. I will not hesitate to recommend this volume to scientists from the disciplines indicated above and also to the general reader with interests in medicinal plants, malaria, and travel medicine. HG

—Maurice M. Iwu, PhD
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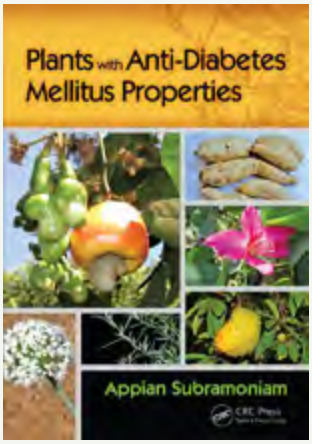
Plants with Anti-Diabetes Mellitus Properties by Appian Subramoniam. Boca Raton, FL: CRC Press; 2016. Hardcover, 591 pages. ISBN: 978-1-4822-4989-7. $239.95.

Diabetes, a serious systemic disease largely caused by lifestyle factors, is on the rise throughout the world. However, traditional plant medicine and localized diets may provide leads for novel and effective therapies. The author's goal in writing this book was to publish a reference containing as much information as possible on the current state of antidiabetic plant research. Ultimately, this book serves to further investigations on plant-based diabetes therapeutics.



The book begins with an extensive overview of diabetes. This includes a background on insulin and glucose homeostatic processes and information about the progress of the disease from abnormal mechanisms in the cell, such as impaired glucose uptake and insulin signaling, to affected tissue in the body and resultant systemic complications. A diagram of insulin signaling and a figure that outlines tissue complications support the information in the text. Current standard medications are reviewed here with descrip-

tions of their mechanisms of action. Additional citations would have helped provide greater background on the available research. The introduction also discusses reasons why plants may yield, or have already supplied, treatments for diabetes and eloquently outlines the goals of this book. Overall, the introductory sections are excellent and provide a basis for understanding the latter sections of the book.

The majority of the text consists of a thorough list of plants investigated and/or used for diabetes treatment. Each entry begins with the plant's Latin binomial and, occasionally, the standard common name. The length of the entries is inconsistent: Some entries include extensive information, such as ethnobotanical histories, research, clinical descriptions and citations, distribution, and pharmacology, but many entries consist of only one short paragraph. However, the author explains that not all plants have been investigated equally and, therefore, some plants are discussed more extensively. Common names, distribution, and traditional uses are basic information that should be included in all entries but, unfortunately, are not.

Of the more extensively discussed plants, the research summaries and phytochemical and pharmacological details presented are particularly thorough. One highlight of this section is the inclusion of a table that lists plants used traditionally for diabetes that have yet to be studied by modern pharmacological methods. That table should be especially pertinent to students or researchers looking for good candidate plants to investigate.

The book closes with a section on nutraceuticals, defined as "medicinal," "functional," or "bioactive" foods. A table lists foods and spices used for the treatment of diabetes and is accompanied by photos for reference. This section also could have been more extensive, since there is a wealth of clinical and basic studies supporting antidiabetic activity of traditionally used foods and spices. A summary of research on the traditional food bitter melon (*Momordica charantia*, Cucurbitaceae), for example, could have justified a whole section. However, the section is useful as a quick reference.

While comprehensive and well-researched, the book has a few notable shortcomings. In the introduction, there should have been a history of metformin, one of the most successful drugs ever discovered for diabetes. Metformin originally was based on a compound derived from goat's rue (*Galega officinalis*, Fabaceae), a plant used in traditional European medicine to treat diabetes. Discussion of this in the introductory sections as a notable example of a plant-based diabetes therapeutic is highly warranted, but only a brief mention of this and a paragraph on the plant are included. The introduction also should have featured the vascular system in the tissue diagram, since cardiovascular diseases are three times as prevalent in the affected population.

I would recommend this book as a worthy investment for graduate students, researchers, or practitioners who need a comprehensive but easily searchable reference of plants with antidiabetic activities. The listed price is high, but a reference such as this could be easily shared in a laboratory or clinic. I envision that this text could be especially helpful to health care providers serving global communities. HG

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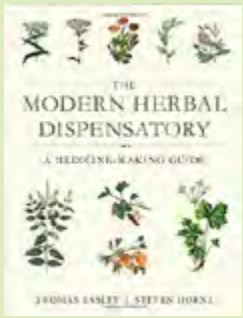
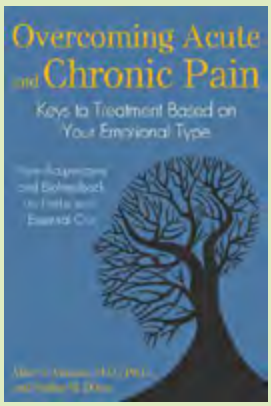
New Book Profiles

The Modern Herbal Dispensatory: A Medicine-Making Guide by Thomas Easley and Steven Horne. Berkeley, CA: North Atlantic Books; 2016. ISBN: 9781623170790. Softcover, 376 pages. $24.95.



A back-to-basics approach with full-color photography, *The Modern Herbal Dispensatory* provides instructions for beginner and more experienced herbal medicine users alike. The text covers a wide array of preparation methods, both for internal and topical use, for almost 250 different herbal medicines. From harvesting to administration, readers can follow along to prepare their own capsules; extracts in alcohol, glycerin, water, vinegar, or oil; and salves, lotions, and poultices. To aid in dosage, the authors provide referenced information that explains how different preparations of the same plant have different effects, which allows the reader to make an informed decision about how to obtain the desired outcome. Essential oils and flower essences also are discussed.

Overcoming Acute and Chronic Pain: Keys to Treatment Based on Your Emotional Type by Marc S. Micozzi and Sebhia Marie Dibra. Rochester, VT: Healing Arts Press; 2017. ISBN: 9781620555637. Softcover, 288 pages. $18.95.

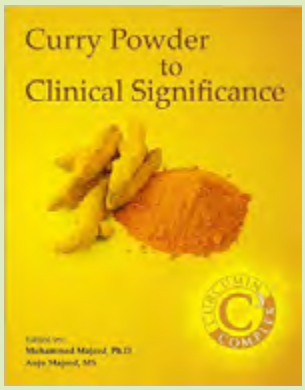


This holistic guide to safe and effective natural therapies allows those who suffer from acute or chronic pain conditions to explore their treatment options based on their specific condition. Marc Micozzi, MD, PhD, and Sebhia Marie Dibra review scientific evidence for mind-body techniques, such as hypnosis and yoga; hands-on healing, including acupuncture and massage therapy; and pain management with natural products, such as herbal remedies and essential oils. The common conditions discussed in the text include arthritis, back pain, fibromyalgia, irritable bowel syndrome, migraines, carpal tunnel syndrome, and post-traumatic stress disorder (PTSD). The information presented in this text is based on the idea of pain as a dynamic condition, and as an interaction between the mind and body, patient and therapy.

Household Medicine in Seventeenth-Century England by Anne Stobart. London, UK: Bloomsbury Academic; 2016. ISBN: 9781472580344. Softcover, 304 pages. $21.99.

Anne Stobart, PhD, examines the question of how early modern households provided their own care to maintain health and treat illness. Drawing from primary documents, such as household papers, Stobart reveals details of how health and disease were managed in 17th-century England. She discusses how remedies both purchased and homemade, which were often made from botanicals, paved the way for modern conventional medicines and health care structures. The issues of health care, wellness, and disease were influenced by a multitude of social factors, such as class, wealth, gender roles, education, and others. This text covers information, resources, and the evolving practice of health care during this time period.

Curry Powder to Clinical Significance by Muhammed Majeed and Anju Majeed, eds. East Windsor, NJ: Nutri-Science Publishers, LLC; 2015. Hardcover, 190 pages. $10.99.



Curcumin, a bioactive component of turmeric (*Curcuma longa*, Zingiberaceae) root, has gained increasing attention and clinical documentation from the scientific and medical communities for its numerous therapeutic activities and potential applications in human health. This book, edited by Muhammed Majeed, PhD, the founder of Sabinsa, a leading India- and United States-based producer and supplier of standardized botanical extracts made from predominantly Indian medicinal plants, and Anju Majeed, MS, a research and development specialist, provides an overview of the clinical studies on Sabinsa's proprietary curcumin extract, Curcumin C3 Complex. The C3 Complex has reportedly been the subject of various clinical trials for more than 26 years for a range of conditions, including inflammation, cognitive health, cancers, and others.

Kathe Koumoutseas 1950-2016

Kathe Koumoutseas, an ardent plant enthusiast, gardener, and former horticultural designer for the United States Botanic Garden (USBG), died at her home on Christmas morning surrounded by her family. She was born Katherine Lagoutaris in June 1950 to Merope Lagoutaris and Panagioti Malliaros on the Greek island of Lesbos ("I'm a true 'lesbian,' as was my father, and grandfather," she would quip.).

At age five, she moved to the United States with her mother. Kathe grew up in Lowell, Massachusetts, and graduated from Lowell High School. She later attended Prince George's Community College in Maryland.

She was a lover of life — particularly herbs and medicinal plants — and was always one to follow her passions and dreams. She collected Indian, Asian, and Native American art, designed and marketed her own label of clothing and accessories, and worked for many years as a designer and horticulturist at the USBG on the main mall in Washington, DC. In the early 1990s, she curated a special exhibition at USBG on ethnobotany and medicinal plants, and, when the garden was closing for a multi-year architectural restoration, she salvaged numerous tropical medicinal plants and sent them for permanent placement at the American Botanical Council's (ABC's) then-new headquarters in Austin, Texas.

"For more than 17 years, thousands of visitors to ABC's historic homestead have directly benefitted from Kathe's gift of many of the beautiful tropical plants formerly at USBG," said ABC Founder and Executive Director Mark Blumenthal. "They receive special care from ABC's garden team, and we are deeply grateful to her for her trust and confidence in ABC's ability to steward them properly."

Kathe also managed the USBG's dinosaur garden, a project that allowed visitors a glimpse at the botanical life on earth from the Paleozoic (542-251 million years ago) to the Mesozoic (251-65 million years ago) eras.

An avid gardener with a green thumb, Kathe's home garden in Fort Washington, Maryland, contained many beautiful ornamental, culinary, and medicinal plants, as well as her beloved wind chime collection.

In recent years, Kathe fulfilled her lifelong dream of journeying to the Amazon as a student of ethnobotany on a National Geographic expedition with the University of Delaware. On the expedition, she cataloged medicinal plants used by the indigenous Ese'Eja tribe and took part in a traditional ayahuasca healing ceremony. Kathe was also active in the movement to legalize medical cannabis (*Cannabis* spp., Cannabaceae) in Maryland and supported organizations dedicated to medicinal cannabis research and education.

A celebration of Kathe's life is planned for March 25, 2017, in Washington, DC. She believed very strongly in causes for social and environmental justice, and donations were made in her memory to the Standing Rock Sioux tribe, the water protectors protesting the Dakota Access Pipeline construction in North Dakota.

Kathe is survived by her son Peter Alexander Koumoutseas; daughter Merope Sophia Moonstone; grandchildren Riley-Grace and James Koumoutseas; life partner Peter Kranz, PhD; stepson Alexander Kranz, his wife Jenny, and their children Isaac and Zachary; and her loving sisters, nieces, nephews, and many cousins. HG

—Jenny Kranz

Robert 'Bob' M. Duggan 1939-2016

Bob Duggan, co-founder and president emeritus of the Maryland University of Integrative Health (MUIH, formerly the Tai Sophia Institute), passed away on October 5, 2016, at the age of 76. Duggan exemplified the pioneering spirit of alternative medicine and fearlessly forged his own path through his life with a deep commitment to his practice. Duggan will be remembered by his colleagues as a national leader for wellness in the United States, a devoted mentor to countless students, and an innovative instructor.

Raised in Manhattan in New York City, Duggan studied widely and earned bachelor's degrees in philosophy and theology, as well as master's degrees in human relations and community studies from New York University, and in moral theology from St. Joseph's Seminary. He also received a master's certification in acupuncture from the College of Traditional Chinese Acupuncture in the United Kingdom. Though he was ordained as a Catholic priest and served in the United States and elsewhere, he left the priesthood in the mid-1960s in order to marry his first wife, Dianne Connelly. Together, Duggan and Connelly formed the Centre for Traditional Acupuncture in Columbia, Maryland, in 1974, one of the first acupuncture clinics in the United States. He continued to practice traditional acupuncture for 44 years at his family-owned and -operated clinic, WisdomWell.

Bevin Clare, an associate professor at MUIH, described how Duggan's philosophy helped form the mission of the university. "Bob influenced herbalists studying at MUIH (then Tai Sophia) through the realization that the work of a clinical herbalist is in fact two distinct interventions: the herbs themselves and the intervention of the practitioner in their words and practices," she wrote. "These concepts are central to many of us in our clinical work and have helped craft us into the practitioners we are today" (email, November 7, 2016).

The Centre evolved over the years into the Traditional Acupuncture Institute (TAI), which launched the United States' second master's program in acupuncture in 1981 and the first accredited program in 1985. TAI changed its name to the Tai Sophia Institute in 2000, and expanded its coursework to include different forms of traditional medicine, including herbal medicine, nutritional therapy, and yoga therapy. In 2013, the institute was granted university ranking from the state of Maryland and changed its name to the Maryland University of Integrative Health. (John Weeks, editor-in-chief of the Integrator blog, notes that these transformations happened "not always with [Duggan's] best wishes."[1])

Weeks's commentary speaks to Duggan's sometimes controversial ideas and how those ideas shaped his relationships with other members of the integrative health community. Mentored in his youth by "maverick" priest and conventional medicine critic Ivan Illich, Duggan's own approach to health care and wellness were often at odds with the institutions and people around him. Duggan's longtime friend and close colleague, Georgetown University law professor Sherman Cohn, wrote: "Some of us will recall Bob's talk to the establishment [residents] of Howard County, Maryland, condemning the upcoming expansion of a major hospital as a total waste of resources. In that talk, as elsewhere, he campaigned for dismantling the medical establishment, not expanding it. It should not be a surprise that many in the audience were in strong disagreement" (email to J. Weeks, October 21, 2016).

"That's Bob," Weeks responded (email, October 21, 2016).

When integrative practitioners debated the issue of licensure for acupuncturists, Duggan suggested that acupuncturists ought to be regulated by local parks and recreation departments instead of professional licensing bodies. He further differed in opinion from certain professional acupuncturists by helping create and promote the Seattle Statement in 1997, a declaration of principles that "[encouraged] collaboration between Acupuncture and Oriental medicine and other individuals and groups within and outside of organized health care systems" rather than keeping acupuncture strictly within the domain of Oriental medicine practitioners.[2]

The spirit of community medicine led Duggan to work extensively with lower-income communities and detention centers throughout Baltimore through Tai Sophia's Community Health Initiative. He brought his insight, experience, and advice to thousands of people, both nationally and internationally through lectures, readings, and workshops, as well as through his two books: *Common Sense for the Healing Arts* (2003) and *Breaking the Iron Triangle: Reducing Health-Care Costs in Corporate America* (2012), both published by WisdomWell Press. Duggan served as a policy advisor and testified before the Senate Committee on Health, Education, Labor and Pensions. He was also a panelist at meetings sponsored by the National Institutes of Health (NIH) and the White House Commission on Complementary and Alternative Medicine. Duggan also served on the board of trustees of The Horizon Foundation and as a chairman for the Maryland State Board of Acupuncture. In 2009, he presented a talk at the first TEDxMidAtlantic conference.

A memorial service for Bob Duggan was held in November 2016 at Penn North Community Resource Center in Baltimore. He is survived by his wife Susan Duggan, children Jade Connelly-Duggan and Blaize Connelly-Duggan, former wife Dianne Connelly, and his grandchildren. Jade, Susan, and Dianne will continue to run WisdomWell according to Duggan's philosophies of wellness and care. HG

—Hannah Bauman

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Christof Jaenicke 1953-2017

Christof Jaenicke, MD, co-founder and chief medical advisor of the Berlin-based international natural products consulting and research firm analyze & realize GmbH, died on January 4, 2017, after a brief battle with pancreatic cancer, just 22 days before his 64th birthday.

Born in Erlangen, Germany, in 1953, Jaenicke founded a publicity agency for musicians at the age of 16, and then studied marketing management and business administration at the Free University of Berlin. After graduating, he switched his course of study to human medicine, receiving a doctorate in medicine and serving as an intern pediatric surgeon at a clinic in Berlin.

Jaenicke entered the world of pharmaceuticals and worked first as the medical director at the Swiss pharmaceutical company Ciba-Geigy, which later merged with another pharmaceutical company to form Novartis, and then in various other positions at other companies, including Sterling-Winthrop, Fresenius, and the phytomedicine company Lichtwer Pharma. At Lichtwer, he met a man who would eventually become his longtime business partner and close friend, European phytomedicine expert Joerg Gruenwald, PhD. Gruenwald and Jaenicke delved into natural products, and developed one of the world's most clinically tested garlic (*Allium sativum*, Amaryllidaceae) products (brand name: Kwai) and the world standard for St. John's wort (*Hypericum perforatum*, Hypericaceae) phytomedicines (LI 160, brand name: Jarsin). With Gruenwald leading the clinical research and Jaenicke leading the marketing, Lichtwer's Kwai and Jarsin became top-selling products in the German market.

After he left Lichtwer, Jaenicke opened Background Consultancy in 1992 and, together with Gruenwald, founded PhytoPharm Consulting in 1996. Over the course of his career, he and Gruenwald established or co-founded more than 20 companies in nine countries around the world.

In the late 1990s, Jaenicke contributed to *The Physician's Desk Reference [PDR] for Herbal Medicines* (Medical Economics, 1998), based on the German Commission E monographs, which quickly became a popular text on the clinical applications of botanicals. He published a companion text in 1999, *The PDR Family Guide to Natural Medicines and Healing Therapies*. From 2003-2006, he and Gruenwald co-authored five more botanical- and phytotherapy-focused reference works.

Jaenicke and Gruenwald founded analyze & realize in 2001, and Jaenicke served first as CEO and, after 2013, as the chief medical advisor. While the company began as a consulting firm that specialized in medicinal herbal products, it eventually expanded its mission to include natural product research, functional food and food supplement development, and clinical study performance. Jaenicke's research focused on functional foods, plant-based ingredients, such as lycopene, and the untapped potential of medicinal plants from Malaysia, Vietnam, and other countries around the globe.

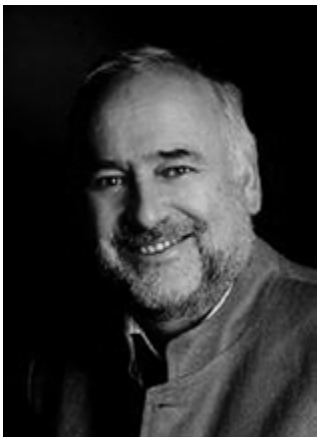
Gruenwald delivered a eulogy for Jaenicke, in which he described him as "racing at high speed … always searching for new challenges and never satisfied with a status quo, his environment, and especially himself…. Christof was always a dominant, space-roving personality, full of spirits, always full of new ideas and plans."

Thomas Hafner, with whom Jaenicke helped found InQpharm, wrote: "Christof was a true friend, a loyal colleague, a tireless fighter and believer in our cause, a brilliant mind, and a true legend in many ways. Whilst he may no longer be with us, his signature on some of our lives and our organization mean that he will stay amongst us forever" (email to J. Gruenwald, January 4, 2017).

Friends and colleagues remember Jaenicke's charisma and natural salesmanship. "When he was selling and negotiating … he always took new arguments out of his sleeve. He simply chattered to people so hard that they gave up and agreed with him," Gruenwald recalled in his eulogy. "But now you are gone, Christof…. I do not know yet how [we] will proceed without you."

Christof Jaenicke is survived by his wife Susanne and his four children. HG

—Hannah Bauman



Klaus Dürbeck
1956-2016

Klaus Dürbeck, Dipl.-Ing. Agr., passed away unexpectedly on December 16, 2016, at the age of 60. For decades, Dürbeck carried out field work around the world as an expert consultant for governmental and intergovernmental organizations on projects to develop value chains for the sustainable management and trade of medicinal and aromatic plants. He also was passionate about volunteerism, and played a leadership role in several non-governmental organizations (NGOs) concerned with quality assurance and the sustainability of medicinal plant production and trade.

Dürbeck was born in Bad Neustadt an der Saale, Bavaria, Germany, on February 1, 1956. After completing basic vocational training in agronomy at the Agricultural Office of Bad Neustadt an der Saale in 1980, Dürbeck studied at the Technical University of Munich in Weihenstephan and graduated in 1984 with a diploma in agricultural engineering (Dipl.-Ing. Agr.).

From 1987 to 1988, Dürbeck served as associate expert for the United Nations Industrial Development Organization (UNIDO) in its Industrial Utilization of Medicinal and Aromatic Plants Programme. Starting in 1988, he perennially carried out medicinal plant and natural ingredients sector assignments as an expert consultant for the German Agency for Technical Cooperation (Deutsche Gesellschaft für Technische Zusammenarbeit, or GTZ*). From 2001 onwards, he also took similar assignments as a senior expert for trade development for organic products and natural ingredients for the Swiss Import Promotion Programme (SIPPO) and as a natural ingredients sector expert for the Dutch Centre for the Promotion of Imports from Developing Countries (CBI).

Klaus Dürbeck Consulting (KDC), founded in 1992, became the mechanism through which Dürbeck carried out medicinal plant field work for governmental development aid projects, most notably working with communities in Asia (Afghanistan, Nepal, Pakistan, Uzbekistan, Vietnam), Latin America (Ecuador, El Salvador, Nicaragua, Peru), and the European Balkans (Bosnia and Herzegovina, Kosovo). KDC is a family business in which Dürbeck mentored and worked alongside his daughter Teresa Hüttenhofer and niece Petra Dürbeck, together with other upcoming professionals in the field.

Dürbeck's commitment to good agricultural and collection practices (GACPs), quality assurance, and sustainability standards for medicinal and aromatic plants often elevated him to leadership roles. In 1996, he became a member of Forum Essenzia eV, a nonprofit association for the promotion, protection, and dissemination of aromatherapy, aromacare, and aromaculture, and served as its president from 2004 to 2009. Over the past 20 years, Dürbeck contributed articles to *FORUM*, the journal of Forum Essenzia, and actively participated in the association's annual congresses, including the most recent in November 2016.[1]

Ingeborg Stadelmann, midwife, naturopath, author, and president of Forum Essenzia, in her eulogy to Dürbeck at his funeral in Raubling, Germany, on December 22, 2016, said:

> After finishing his term as president, he remained at our disposal as an advisory board member, always willing to offer advice. Not one email remained unanswered and some of his responses were sent from distant, crisis-stricken countries.... Klaus led the association in a future-oriented manner, blazing new trails and also giving shape to them, for example, by connecting countries of origin, trade, science, and therapeutic application. He sought out and established international contacts from the distillers to scientists and pharmacists, to the end-users of essential oils. Thanks to his lobbying and tireless dedication in the countries of origin, we now have many precious, unadulterated essential oils available in Europe. He played an important role in raising awareness of sustainability and wild-collection among essential oil professionals.

In addition to his fascination with the ecology and biochemical properties of medicinal plant species, Dürbeck was deeply committed to supporting the needs of entrepreneurs in developing countries, as illustrated through his long engagement with the development of trade standards for wild plant products. Version 1.0 (November 2006) of the FairWild Standard, an international standard for sustainable harvesting and trade of plants, fungi, and lichens, was developed collaboratively through the support of Forum Essenzia (represented

* As of January 1, 2011, GTZ merged with two other agencies to become the German Agency for International Cooperation (Deutsche Gesellschaft für Internationale Zusammenarbeit, or GIZ).

by Dürbeck), the Institute for Marketecology (IMO), and SIPPO. In 2008, Dürbeck became a founding member of the FairWild Foundation, a Swiss nonprofit organization responsible for the FairWild Standard and certification process, and served as president of its board of trustees. In this role, he made an immense contribution to the work of the foundation, overseeing the merging of the original FairWild Standard with the International Standard for Sustainable Wild Collection of Medicinal and Aromatic Plants (ISSC-MAP) and engaging stakeholders in the implementation of the resulting FairWild Standard v2.0.

His legacy was underlined in the obituary announcement from the FairWild Foundation: "With his dynamic personality and drive, Klaus was a key leader of our Foundation who will be hugely missed. In losing Klaus, we have lost a true champion of our shared goals and values, and a great friend. His passion for FairWild, medicinal plants, and the sustainable livelihoods of harvesters worldwide will be remembered for many years to come."[2]

Dürbeck also served as an appointed bureau member (treasurer) of the International Council for Medicinal and Aromatic Plants (ICMAP), an NGO established in 1993 to promote "international understanding and cooperation between national and international organizations on the role of medicinal and aromatic plants in science, medicine and industry, and to improve the exchange of information between them."[3]

The often-cited book *The Distillation of Essential Oils: Manufacturing & Plant Conservation Handbook,* co-authored by Dürbeck (with R.O.B. Wijesekera, PhD, and C.M. Ratnatunga), was published in 1993 by the GTZ Protrade.[4] Most recently, Dürbeck co-authored, with his daughter Teresa, a book chapter titled "International Trade of Medicinal and Aromatic Plants" for the first volume of a new book series titled *Medicinal and Aromatic Plants of the World*.[5]

K. Hüsnü Can Başer, PhD, a professor of pharmacognosy at Near East University in Nicosia, Cyprus, and the vice-president of ICMAP, wrote: "I had known him for the last 30 years, since I first met him at UNIDO Headquarters when he was assistant to Dr. R.O.B. Wijesekera. He has devoted all his life to helping herbal producers in developing countries…. His demise is also a great loss for the ICMAP family" (email to M. Blumenthal, December 20, 2016).

Dürbeck's passion and energy for his profession remained until his last day. On the morning of his untimely death, he was to have a breakfast meeting to discuss future projects with his friend Beat Kündig, owner of Zürich-based W. Kündig & Cie AG, an international distributor of conventional as well as organic-, Fairtrade-, and FairWild-certified natural ingredients that was founded in 1920. "It is always difficult to say something about a person like Klaus without getting too emotional," wrote Kündig (email to J. Brinckmann, December 27, 2016). "He was tolerant, witty, had great expertise (which he enjoyed sharing with others) and he had a very big heart. It always gave me great pleasure to collaborate with him." Kündig also spoke at the funeral service.

Dürbeck did not just enjoy sharing his expertise with others, but was determined to transmit knowledge to the next generation, and strongly encouraged his colleagues to join him in that effort. Since 2004, he had hosted an annual "Inner Circle – Outer Circle" (ICOC) workshop inviting selected young, aspiring consultants to participate and engage in medicinal and aromatic plant project work with seasoned experts. Stadelmann, an ICOC participant, wrote: "At the funeral, everyone agreed that ICOC 2017 should proceed in accordance with Klaus' wishes" (email to J. Brinckmann, December 24, 2016).

Dürbeck will be remembered not only as a true expert in his field, but also as a lifelong friend. "Ever since we met some 20 years ago, Klaus has been a great companion in my work and life," wrote Bert-Jan Ottens, managing director of ProFound, a consultancy firm, and fellow FairWild Foundation board of trustees member (email to J. Brinckmann, December 27, 2016). "Starting with concepts for non-wood-forest-products, we ventured into national BioTrade programmes, to more recently develop FairWild certification concepts for a multitude of natural ingredients for food, cosmetics, and pharmaceuticals. These concepts are now being implemented in many programmes and projects. In 2014, we co-founded 'IN2NI,' an international network of experts promoting sustainable sourcing of natural ingredients. Klaus was our master in the world of medicinal and aromatic plants, and he will be hugely missed. We are bound to carry on with his legacy."

His loss will be keenly felt by his family, friends, and many colleagues around the world. As Stadelmann said: "Klaus, it is simply unbelievable that you are no longer with us, that you will no longer board the airplane, but rather are now here in your beloved native land, your final resting place in the Bavarian Inntal Valley."

Klaus Dürbeck is survived by his wife Gertrud; his children Teresa, Benedikt, and Marian; his mother Lioba Dürbeck; and his brothers and sisters. HG

—Josef Brinckmann

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Publications

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

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

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

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Photo taken by Beth Ebbing Johnson, co-founder and owner of Sacred Moon Herbs in Dripping Springs, Texas. Photograph captured with a Nikon D5100 at 55mm f8, 1/60sec, ISO 100.

Borage

Borago officinalis, Boraginaceae

Native to the Mediterranean region, borage (*Borago officinalis*, Boraginaceae) is cultivated for its seed oil and has edible aerial parts with distinctive star-shaped blossoms. Due to the cucumber-like flavor of its greens, borage has a widespread culinary use throughout the Mediterranean in salads and sauces. In the United Kingdom, the flowers are a traditional ingredient in cocktails such as claret cup and Pimm's cup. Borage's medicinal history stretches back to the ancient Greek tradition of healing, as borage is mentioned by Dioscorides and Pliny the Elder.[1] Traditionally, borage has been used for gastrointestinal, asthmatic, and cardiovascular conditions, and modern uses also include the treatment of hormonal conditions, such as menopause and premenstrual syndrome.[2] The seed and herb contain potentially hepatotoxic pyrrolizidine alkaloids; in borage seed oil, these alkaloids may be removed during the refining process.[3,4]

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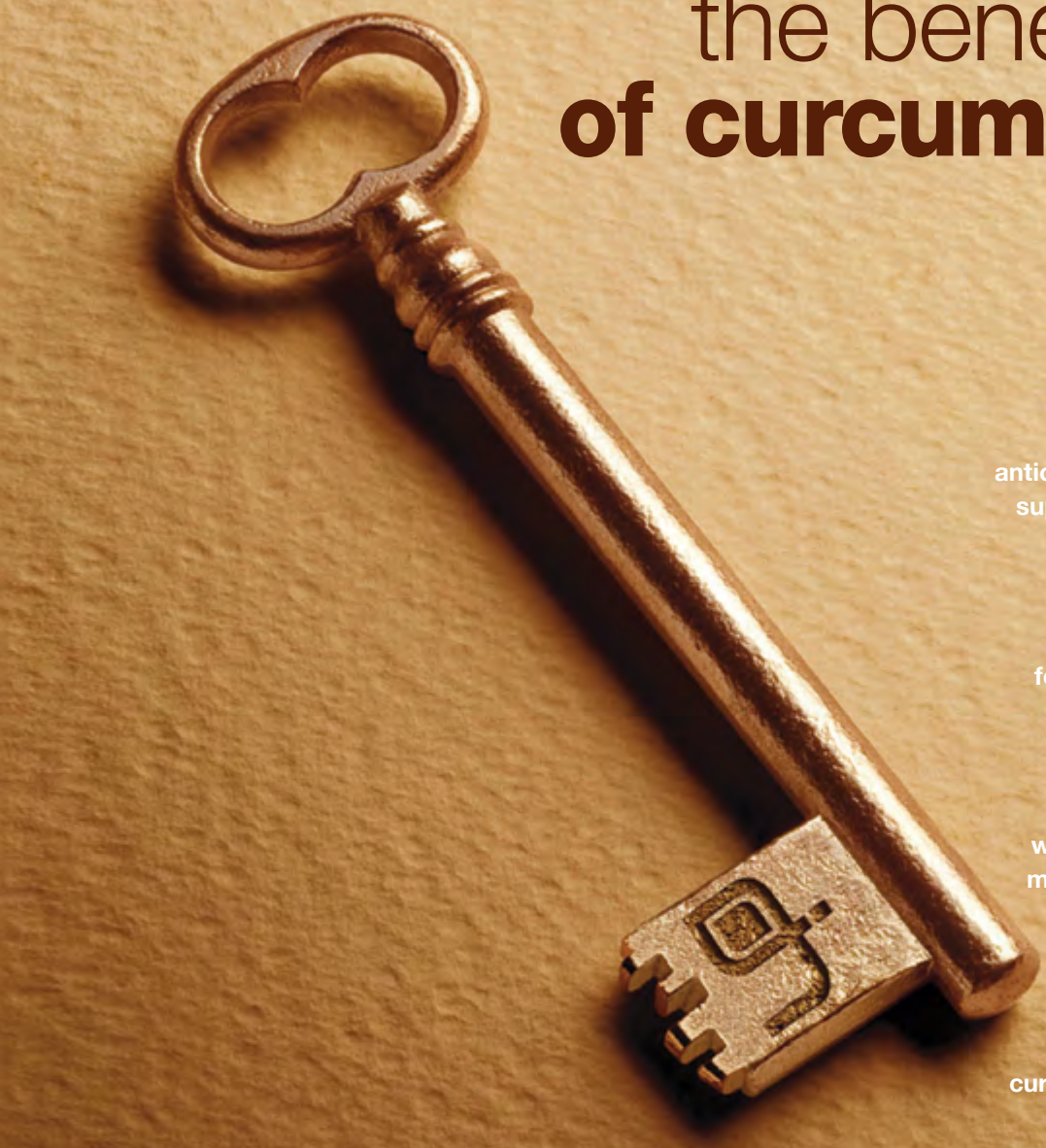

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