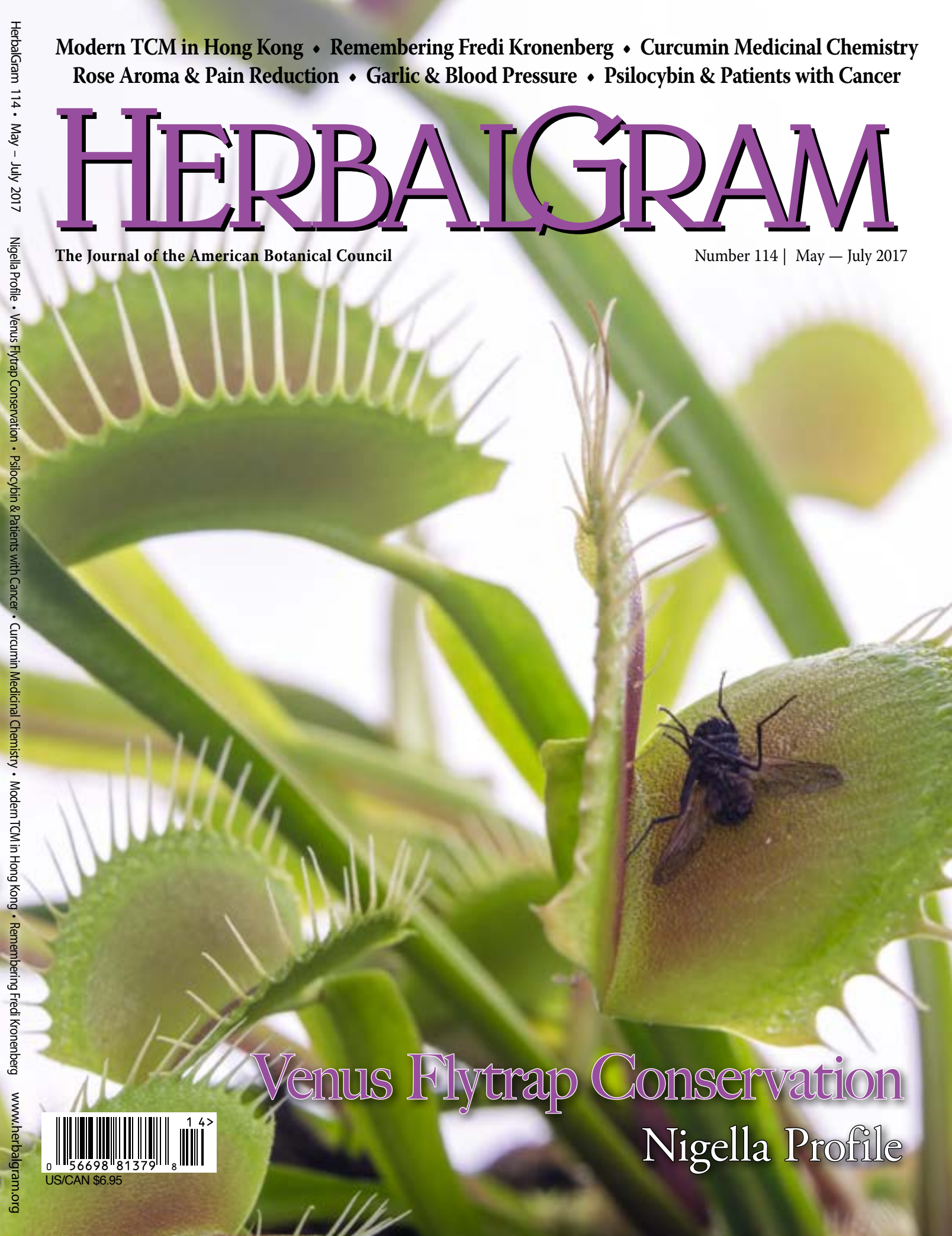
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Modern TCM in Hong Kong • Remembering Fredi Kronenberg • Curcumin Medicinal Chemistry
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# HERBALGRAM

The Journal of the American Botanical Council

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# dear *reader*

Of the myriad ways plants have adapted to their environment, none are more curious than carnivorous plants — plants such as the Venus flytrap and pitcher plants that have developed anatomical structures and chemistries that allow them to attract, trap, and digest insects and other arthropods. Our cover story this issue features the amazing Venus flytrap, the inspiration for the man-eating plant in the original 1960 movie *The Little Shop of Horrors*. Although they have limited documented medicinal value — some have claimed anti-cancer effects of a proprietary extract of the plant — Venus flytraps are considered threatened in their habitats in a relatively small area of the eastern United States. *HerbalGram* Assistant Editor Connor Yearsley documents the current vulnerability of these curious creatures.

ABC's Gayle Engels and Traditional Medicinals' Josef Brinckmann provide an extensive profile on nigella, or black cumin, an herb that has been used as both food and medicine since ancient times. As nigella becomes increasingly popular in the United States and elsewhere, new research is emerging on its potential use for a variety of conditions, including asthma and rheumatoid arthritis.

According to our annual herb market reports, turmeric has been the top-selling herbal dietary supplement in the US natural food retail channel for the past four years. Turmeric supplements often consist of extracts standardized to certain levels of compounds collectively referred to as curcuminoids, or simply "curcumin," and sales have been driven by reports of anti-inflammatory effects and other potential benefits as shown in a growing body of published clinical trials. A critical review of curcumin for its potential use *as a purified compound* for development as a conventional pharmaceutical drug was recently published in the *Journal of Medicinal Chemistry*, and it concluded that curcumin is not a likely conventional drug candidate. However, the authors left the door open for possible benefits of chemically complex turmeric and curcumin standardized extracts. Media reports of this research erroneously announced that turmeric has no health value. We attempt to clarify this confusion in our Research Review section.

In recent years, there has been increased research on the potential medical benefits of hallucinogenic substances, such as psilocybin, which is derived from fungal species of the genus *Psilocybe* and other genera. Yearsley provides a review of two recent clinical trials on psilocybin for the reduction of anxiety and depression in patients with life-threatening cancer.

Western-trained natural products chemist and pharmacognosist Edward Kennelly, PhD, a member of the ABC Advisory Board, recently completed his Fulbright Scholar Program in Hong Kong. In one of our featured articles, Kennelly and colleague Clara Lau, PhD, a pharmacognosist and expert in traditional Chinese medicine, share their perspectives on the development and modernization of traditional Chinese herbal medicine in one of the world's most modern cities.

In March, the 2016 ABC Excellence Awards were presented at the 12th annual ABC Botanical Celebration and Awards Ceremony at the Natural Products Expo West trade show and conference in Anaheim, California. As usual, we provide a narrative and photos of this event. Of particular note is that the ABC Norman R. Farnsworth Excellence in Botanical Research Award was granted to Her Excellency Ameenah Gurib-Fakim, PhD, the President of the Republic of Mauritius. This marks the first time that one of our awards has been given to a head of state. President Gurib-Fakim is an advocate for African medicinal plants, and she has been a member of the ABC Advisory Board for many years.

Finally, we are deeply saddened to include in this issue a tribute to our dear friend and colleague, the late Fredi Kronenberg, PhD. Among her many other activities and accomplishments, Fredi was a pioneer in the area of complementary and alternative medicine research for women's health, and she served on the ABC Board of Trustees for 18 years, from 1999 until her death in April. Fredi co-founded and directed the Rosenthal Center for Complementary and Alternative Medicine at Columbia University, and, for 10 years, she directed the week-long botanicals training course for physicians and other health care providers at Columbia. Our extensive tribute by *HerbalGram* Associate Editor Hannah Bauman attempts to document her significant influence in the fields of botanicals, nutrition, and integrative medicine. Her positive impact has been immeasurable. ABC and the natural medicine community at large owe her our heartfelt gratitude for her life of service to us all. HG



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## A Snapshot of the Modernization of Traditional Chinese Medicines in Hong Kong: A Fulbright Scholar's Perspective
**By Edward J. Kennelly, PhD, and Clara B.S. Lau, PhD**

The autonomous region of Hong Kong is ranked among the most modern and densely populated cities in the world. Western-style physicians and clinics are commonplace, but many of Hong Kong's more than seven million residents turn to traditional Chinese medicine (TCM) for their health care. As part of an eight-month Fulbright Scholar Program, Edward Kennelly, PhD, a professor of biological sciences at Lehman College in New York, collaborated with local experts and conducted extensive field research and interviews to learn more about the evolution of TCM practice in Hong Kong. Kennelly witnessed a trend toward the modernization of many aspects of TCM practice, from the use of computerized instruments to formulate TCM herbal prescriptions to the proliferation of easy-to-consume preparations such as granules. However, these high-tech advances are not universally preferred, Kennelly explains, and many practitioners still embrace more traditional forms of Chinese medicine.

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## The Venus Flytrap: Conserving the Carnivorous Curiosity
**By Connor Yearsley**

In his book *Insectivorous Plants*, Charles Darwin wrote that the Venus flytrap "is one of the most wonderful [plants] in the world." Now, that "wonderful" plant is being threatened in the wild by a combination of poaching, overharvesting, habitat loss, fire suppression, wetland drainage, seed collection, and other factors. The plant, which grows in a limited area around Wilmington, North Carolina, has been entirely eliminated from large portions of its original range, and some experts consider many of the limited remaining populations too small to prove viable in the long term. Although many of the remaining flytraps occur on protected lands, these plants are still highly vulnerable. Increased conservation efforts are necessary to protect this carnivorous curiosity in the wild.



**Venus flytrap** *Dionaea muscipula*
Photo ©2017 Calyponte



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**Venus flytrap** *Dionaea muscipula*
Photo ©2017 PhotoCPL (iStockPhoto.com)

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# Nigella

***Nigella sativa***

Family: Ranunculaceae

## INTRODUCTION

The genus *Nigella* is relatively small and contains about 18 species with several sub-species[1] and numerous genotypes.[2] All *Nigella* species are therophytes: annuals that complete their life cycle in a short favorable period and survive harsh periods as seeds.[3] *Nigella sativa*, perhaps the most well-known member of the genus, grows 8-35 inches (20-90 cm) in height and has finely divided, somewhat threadlike leaves. This species has pale-blue to pale-purple flowers that bloom in the spring and produce seed capsules (fruit) that contain numerous black seeds.[4]

The genus likely originated in parts of the eastern Mediterranean, northeastern Africa, and southwestern Asian regions.[5,6] *Nigella sativa* is found growing wild in regions of northern Africa,[7] Turkey, Syria, Iraq,[8] and Iran.[9] The species is also cultivated on a commercial scale in northern Africa (Egypt,[10] Tunisia,[11] Sudan[12]), eastern Africa (Ethiopia[13,14]), western Asia (Iraq,[11] Israel,[15] Jordan,[16] Lebanon,[17] Syria,[18] Turkey,[10] Yemen[19]), and southern Asia (India,[20] Iran,[21] Pakistan[22]).

The majority of the global commercial supply of *N. sativa* seed is obtained from cultivation in Egypt, Turkey,[18] and India.[12] In India, it is mainly grown in the far northern states of Punjab, Himachal Pradesh, Bihar, and Assam.[23] Also cultivated extensively in Iran,[24] *N. sativa* is traditionally farmed by communities situated in the provinces of Fars, Khorasan, and Qazvin.[21] Most of the certified organic *N. sativa* seed in the global market originates from farms in Egypt's El-Fayoum agricultural area in the Nile Valley,[10] although there is some organic production in Turkey and India. It should be noted that in Turkey many farmers plant the seeds of *N. damascena* in the same fields with *N. sativa* (email from K. Hüsnü Can Başer, April 5, 2017).

## HISTORY AND CULTURAL SIGNIFICANCE

The common name and genus name *Nigella* is derived from the Latin *niger*, meaning "black." The term *nigellus* is a derivative that means "blackish" or "dark." The species name *sativa*, meaning "cultivated,"[25] is not surprising given that *N. sativa* had been cultivated for thousands of years before Swedish botanist Carl Linnaeus named it in 1753.[26]

In the United States, the preferred standardized common name for *N. sativa* is simply "nigella," according to the second edition of the American Herbal Products Association's *Herbs of Commerce*.[27] *Nigella sativa* is also known as black cumin, black caraway,[28] and black seed,[8] although the common names "cumin" and "caraway" may be misleading, as these names refer to common spice plants (*Cuminum cyminum* and *Carum carvi*, respectively) in the carrot, or Apiaceae, family. One of *N. sativa*'s main trade names, *kalonji*, is also the name used in the Arabic Unani-Tibb system of medicine.[29]

Several archeological sites in Egypt provide evidence of human use of *N. sativa* seed from 1324 BCE through the time of the annexation of Egypt by the Romans in 30 BCE.[30] There is also evidence of cultivation, culinary use, and medicinal use in Mesopotamia from the late third millennium BCE until the late first millennium BCE.[5] Cuneiform tablets of ancient Assyria (comprising parts of present-day Iraq, Iran, Syria, and Turkey) describe various uses for *N. sativa*, including for cases of "a ghost lying on the patient," which called for fumigation with a preparation made from 10 shekels (approximately 110 g) of nigella seed.[31] Believed at the time to be useful for the afterlife journey, nigella seeds were placed in the tomb of Egyptian pharaoh Tutankhamun (ca. 1332-1324 BCE).[2] At the ancient Anatolian Boyalı Höyük archeological site, in the present-day Turkish province of Çorum, a pilgrim's flask (*ampulla*) from ca. 1650 BCE (the Old Hittite Period) was found to contain a cache of *N. sativa* seeds mixed with bee propolis and beeswax. While *N. sativa* seeds are traditionally taken with bee products in this region, this may be the first archeological evidence of the combination.[32] There is also evidence of Levantine-Aegean trade in *N. sativa* seed during the Late Bronze Age. Excavations of the Uluburun shipwreck, which occurred sometime between 1350 BCE and 1300 BCE off the Mediterranean coast of present-day Turkey, uncovered *N. sativa* seeds contained in Canaanite amphorae (tall, narrow-necked jars with handles).[33] The use of nigella seed was described in the Book of Isaiah 28:25-27 of the Hebrew Bible as well, which dates back to the eighth century BCE.[15]

In his *De Materia Medica*, Greek pharmaco-botanist Dioscorides (40-90 CE) described the black seeds of a plant he called *melanthion* (now believed to have been *N. sativa*) for use as food (sprinkled on bread) or as a treatment for difficult breathing (when drunk with soda), headaches (applied to forehead), toothaches (boiled with vinegar and pitch pine; used as mouth wash), imperfections of the skin, leprosy (applied with vinegar), incipient cataracts (applied in the nostril as an unguent [an ointment or lubricant] made from iris [*Iris* spp., Iridaceae]), and catarrh (as nasal inhalant). Dioscorides also described the use of melanthion to remove corns (applied with old urine to incised corns), expel roundworms (applied by smearing with water), stimulate menstruation and urination, and repel snakes (fumigation).[34] Fragments of cultivated plant remains of *N. sativa* (both carbonized and desiccated seeds) have been identified at archeological sites in the eastern desert of Egypt, Mons Claudianus,[35] a Roman quarry settlement inhabited during the late first and second centuries, and Mons Porphyrites, another Roman mining site.[36] During the same period, Romans brought nigella seed with them



*Nigella sativa*
Photo ©2017 K. Yamada



Above: Examples of amphorae being removed from the seabed of the Uluburun archeological site after careful documentation. Some of these recovered amphorae were found to contain *N. sativa* seeds.

Below: Amphora and large gold chalice with a pedestal base.



Photos ©2017 Institute of Nautical Archaeology

to western European outposts. Excavation of the second century Roman settlement of Oedenburg (in the lower plains of the Rhine River in Germany) turned up mineralized seeds of *N. sativa* — a rare archeological finding that indicates *N. sativa* seed was important enough to be imported from the Mediterranean.[37,38]

Nigella seed is widely used in the traditional Ayurvedic,[23] Siddha,[39] and Unani[29] systems of medicine, as well as in oral-tradition folk and tribal medicines of India.[40] It is also used in traditional Arabic and Islamic medicine (TAIM),[41] Iranian traditional medicine (ITM),[42] and traditional Sudanese medicine,[43] among other systems of medicine. Medicinal uses of nigella seed (Arabic name: *hubatul-sudda*) were also described in the *hadith* literature, attributed to the Islamic Prophet Muhammad and compiled during the eighth and ninth centuries.[44] A claim that nigella seed is a medicine for every disease except death has been attributed to the Prophet Muhammad.[13,45] In TAIM practice, both the seed (taken with honey) and the fatty oil are used for treating a range of intestinal disorders and respiratory tract conditions.[41] In ITM, nigella seed (Persian names: *shoneez*, currently *siahdaneh*) is used in some herbal preparations to treat epilepsy.[46]

*Nigella sativa* is still widely used in Asian systems of medicine. As such, quality standards monographs providing specifications and test methods for *N. sativa* seed have been published in the *Ayurvedic Pharmacopoeia of India*,[23] *Siddha Pharmacopoeia of India*,[39] and in the *Unani Pharmacopoeia of India*.[29] The United States Pharmacopeial Convention proposed the development of a "Nigella Sativa Seed" monograph for its *Herbal Medicines Compendium* in May 2013. A draft version of that monograph is posted online with a call for submission of validated information needed to complete the monograph.[47] India's Ministry of Agriculture also has established national grade designations and quality standards for the dried, whole, mature seeds of *N. sativa* (Hindi name: *kalonji*), as well as for the powdered seed for use as a spice. Among other specification requirements, "special grade" kalonji seed must contain minimum 1.5% (v/w) essential oil while "standard grade" kalonji must contain minimum 1.0% (v/w) essential oil.[48] In 2014, India, through the Codex Alimentarius Committee on Spices and Herbs, proposed the development of an international codex standard for cumin, including both *N. sativa* and brown cumin (*Cuminum cyminum*), with a goal to finalize it by July 2017.[49]

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

In countries where the Ayurvedic system of medicine is recognized and practiced (e.g., India, Bangladesh, Bhutan, Malaysia, Nepal, and Sri Lanka), the powdered dried seed of *N. sativa*, referred to as *upakuncika* in Sanskrit, is used as a component of preparations for treating abdominal distention with gas, gaseous tumor of the abdomen, diarrhea, and worm infestation.[23] Where the Unani system of medicine is recognized and practiced (e.g., Bangladesh, India, Malaysia, Pakistan, and Sri Lanka), the dried seed is used as a component of medicinal formulations to treat asthma, colic, flatulence, weakness of the stomach, hemicrania continua (persistent unilateral headache) and migraine, arthralgia (joint pain), lumbago (lower back pain), hemiplegia (paralysis of one side of the body), Bell's palsy (paralysis on one side of the face), jaundice, pityriasis (patches on skin), and leukoderma/vitiligo (loss of skin pigmentation). Kalonji is often dispensed as a component of compound Unani medicines known as *majoon* or *halwa*. These soft or semi-solid preparations are made with powdered botanicals and mixed with honey, resulting in a consistency like that of the popular confection halva.[29] In Siddha medicine — a Dravidian system of medicine originating in the southeastern Indian state of Tamil Nadu, now also practiced in the neighboring states of Karnataka, Kerala, and Andhra Pradesh, as well as in parts of Malaysia, Singapore, and Sri Lanka — the dried seed, referred to as *karuncirakam* in Tamil, is used as a component of formulations indicated for treatment of conditions including painful gastrointestinal disorders with indigestion, flatulence, jaundice, scalp eczema, scabies, and skin ulcers.[39]

In the United States, the Food and Drug Administration (FDA) classifies "black cumin (black caraway), *Nigella sativa* L." as Generally Recognized as Safe (GRAS) for use as a spice, natural seasoning, or flavoring.[28] Nigella is also permitted as a component of dietary supplement products, which require FDA notification within 30 days of marketing if a structure-function claim is made and product manufacturing that conforms with dietary supplement current Good Manufacturing Practices (cGMPs).[50]

In Canada, both *N. sativa* seed and seed oil are regulated as medicinal ingredients of licensed natural health products (NHPs, a category of drugs), which require pre-marketing authorization from the Natural and Non-prescription Health Products Directorate. At the time of this writing (April 2017), there were 85 licensed NHPs that list some form of *N. sativa* as an ingredient, of which 78 list it as a medicinal ingredient and seven as a non-medicinal ingredient.[51]

For use in cosmetic products, the European Commission Health and Consumers Directorate lists "Nigella Sativa Seed Extract" for perfuming and skin-conditioning functions, and "Nigella Sativa Seed Oil" (fixed oil expressed from the seeds of *N. sativa*) for emollient, perfuming, and skin-conditioning functions.[52]

## MODERN RESEARCH

There is significant genetic variation and quantifiable differences in chemical and nutrient composition among *N. sativa* seed chemotypes of Egyptian, Iranian, Syrian, and Turkish origin.[53] Such differences may also exist in chemotypes found within a single country. In India, for example, samples of *N. sativa* seed obtained from 10 different states showed significant variation in chemical constituents and morphology.[54]



HERB PROFILE

The primary constituents in *N. sativa* seed are fatty oils (30-35%), mainly glycerol esters of linoleic, oleic, and palmitic acids, and aliphatic hydrocarbons, arachidonic acid (0.01-0.4%), γ-linolenic acid (0.1-1%), and tocopherols (about 170 mg/kg). The seed also contains essential oil (0.4-2.5%), which is composed mainly of monoterpenes, including ρ-cymene, thymoquinone, α-pinene, and carvacrol. The chemical nature of the constituents nigellone and nigellin remains unclear. Nigellone, described as a component of the essential oil, is possibly a polymer of thymoquinone, while nigellin has been described as an alkaloid. There are also traces of isoquinoline alkaloids (nigellicine and nigellimin-N-oxide), an indazole-type alkaloid (nigellidine-4-*O*-sulfite), and dolabellane-type diterpene alkaloids (nigellamines A1 to A5, B1, B2, and C).[55] Analysis of essential oil composition can distinguish *N. sativa* and *N. damascena*. The essential oil of *N. damascena*, which is used in perfumery, contains approximately 8-10% of damascenine, a blue-fluorescing alkaloid. *Nigella sativa* essential oil does not contain this compound and therefore shows no fluorescence (email from K. Hüsnü Can Başer, April 5, 2017).

In vivo and in vitro studies have shown nigella seed powder and oil to have antibacterial, antifungal, antihistaminic, antihypertensive, anti-inflammatory, antinociceptive, antioxytocic, antiparasitic, antiviral, diuretic, hematological, hepatoprotective, hypoglycemic, immunopotentiating, wound-healing, and respiratory-stimulant properties.[54,56]

At least 38 clinical studies have investigated *N. sativa* seed and seed oil for their efficacy for various conditions, including respiratory, diabetic, hepatic, metabolic, mental, and dyspeptic disorders, male infertility, and others.

One 2017 prospective, phase II, randomized, double-blind, placebo-controlled (RDBPC) study explored the effects of cold-pressed *N. sativa* oil (NSO; 0.7% thymoquinone; Marnys Cuminmar; Cartagena, Spain) on subjects with asthma. For four weeks, participants (N = 80) took either 500 mg of NSO twice daily or placebo. Compared to placebo, the NSO group showed a significant improvement in mean Asthma Control Test scores, as well as a significant reduction in blood eosinophils, which play a major role in asthma inflammation. There was a trend toward improved pulmonary function and peak expiratory flow in the NSO group that did not reach statistical significance, and there was no significant change in total serum immunoglobulin E (IgE) levels between groups. The authors recommend that "future studies should follow patients for a longer period and use additional outcomes to validate the benefits of NSO in asthma."[57]



*Nigella sativa*
Photo ©2017 Pamela J. Eisenberg

Another RDBPC study, published in 2008, evaluated the effects of a boiled aqueous extract of nigella seed (NS; 50 mg/mL; no additional information provided) on subjects with respiratory symptoms including chest tightness, breathlessness, cough, and wheezing as a result of chemical inhalation. The participants (N = 40) were an average of 48.2 ± 11.91 years old and the exposure had occurred 18-20 years previously. Each participant drank either the NS extract (0.375 mL/kg of body weight) or a placebo solution daily for two months. Participants received medical exams wherein respiratory symptoms were measured at baseline, 30 days, and the end of the intervention. There were no significant differences between groups at baseline. Significant improvements in all symptoms were seen in the NS group at visits two (day 30) and three (day 60) compared to baseline, except for morning wheeze and cough at day 30. All symptoms were significantly improved by the end of the study compared to day 30 in the NS group. Additionally, all symptoms were significantly reduced in the NS group at day 30 and the end of the study compared to placebo.[58]

Six additional studies have investigated the effects of nigella on respiratory issues. Three of these studies addressed allergic rhinitis: One study found no significant improvement with 0.6-0.8 mg/kg NSO three times daily over six weeks[59]; one found significant improvement in symptoms over one month with 2 g NS once daily[60]; and one claimed improvement in symptoms with NSO but did not specify the dosage.[61] Another study on asthma, which tested 1 and 2 g/day of NS, found that both doses resulted in significant improvements in markers at six and 12 weeks compared to baseline.[62] One study on lower respiratory tract illness in children reported significant improvement compared to baseline in pulmonary index scores and some improvement in peak expiratory flow rate with daily administration of NSO (0.1 mL/kg of body weight) over 14 days.[63] Finally, one study that investigated the effect of a NSO nasal spray (22 mg cold-pressed NSO/25 mL spray) on nasal symptoms in elderly patients for two weeks found that nasal dryness, obstruction, and crusting improved significantly with NSO treatment compared to a saline solution.[64]

At least two studies have assessed the effects of nigella on patients with rheumatoid arthritis (RA). In one RDBPC study from 2014, patients with RA (N = 42) were randomly assigned to receive either 500 mg NSO (produced by Barij Essence Pharmaceutical Co.; Kashan, Iran; soft gel capsules containing 500 mg of cold-pressed NSO) or placebo (paraffin) twice daily for eight weeks. Blood samples were taken at baseline and the end of the study to measure markers of inflammation (serum tumor necrosis factor alpha [TNF-α] and interleukin 10 [IL-10]) and oxidative stress (serum malondialdehyde [MDA] and nitric oxide [NO]). The NSO group experienced a significant increase in serum IL-10, and a significant decrease in serum MDA and NO, compared to placebo. No significant changes in other biomarkers were observed between or within groups. Nevertheless, these results suggest that NSO could be a valuable adjunct therapy in RA, as it improves certain markers of inflammation and oxidative stress in patients.[65]

Another placebo-controlled study, published in 2012, investigated the effects of nigella in female patients with RA. After taking starch-filled placebo capsules twice daily for one month, subjects (N = 40) took 500 mg of cold-pressed NSO twice daily for an additional month. Investigators reported significant improvements in the patients' Disease Activity Scores (a clinician-rated measure of joint swelling and tenderness) compared to ratings taken both before and after the one-month placebo period.[66]

At least two studies have investigated the impact of nigella on mental and cognitive health. In one 2013 RDBPC clinical trial, 40 healthy elderly volunteers were randomly assigned to take 500 mg crushed and encapsulated NS (no additional information provided) or placebo twice daily for nine weeks. Compared to baseline, the test group experienced significant differences in scores on various measures of memory, attention, and cognition, including logical memory tests I and II, a digit span memory assessment (total score), and the Rey-Osterrieth complex figure test (30-minute delayed recall and percent score). There were also significant differences compared to baseline in the time taken to complete a letter cancellation test and trail-making tests A and B. The authors suggested that additional studies should be undertaken with large populations of patients with Alzheimer's disease over a longer period of time to determine if NS can enhance memory, attention, and cognition in that population.[67]

Another RDBPC study explored the effectiveness of nigella in treating mood, anxiety, and cognition. Young men (N = 48; 14-17 years old) were randomly assigned to take 500 mg crushed and encapsulated NS (no additional information provided) or placebo daily for four weeks. Compared to baseline, there was a statistically significant improvement in scores on the Bond-Lader visual analog scale (a measure of mood) for the NS group, but no statistically significant difference between the NS group and placebo group. There was also a statistically significant decrease in State-Trait Anxiety Inventory scores in the treatment group over four weeks compared to placebo. Both immediate free recall and delayed recall improved significantly over four weeks in the treatment group only. The authors postulated that cognition may have improved due to the improvements in anxiety and mood, and suggested that further long-term studies are warranted.[68]

A 2016 RDBPC study examined the effect of nigella on Hashimoto's thyroiditis, an immunological condition that impacts the thyroid gland. Patients with Hashimoto's (N = 40) were randomly assigned to take 2 g of ground NS (prepared by Goldaru Pharmaceutical Co.; Isfahan, Iran; no additional information provided) daily or placebo. The NS group experienced significantly reduced body weight, body mass index (BMI), and hip and waist circumference over eight weeks compared to the placebo group. Additionally, serum concentrations of thyroid stimulating hormone (TSH) and anti-thyroid peroxidase (anti-TPO) antibodies decreased in the NS group over eight weeks, while serum triiodothyronine (T3) increased. While there was no change in the concentration of nesfatin-1 (a neuropeptide involved in the regulation of hunger and fat storage) during the study, the authors noted that changes in anthropometric variables (weight, BMI, and hip and waist circumference) and thyroid hormones (TSH, anti-TPO, and T3) are often significant predictors of changes in nesfatin-1 concentrations.[69]

In a 2014 randomized, double-blind, controlled trial, NSO (verified seeds, dried, ground, and extracted with 96% ethanol, which was later evaporated) was compared to fish oil for the treatment of vitiligo, a condition characterized by a loss of skin pigmentation. Patients with vitiligo (N = 52) were randomly assigned to apply NSO or fish oil on lesions twice daily for six months. By the end of the study, Vitiligo Area Scoring Index (VASI) scores had improved significantly in the NSO group compared to the fish oil group. There were no significant changes in VASI scores between groups in the first three months; not until the fourth month of the study did significant improvement appear in the NSO group.[70]

A 2016 randomized, triple-blind, placebo-controlled trial investigated the effectiveness of NSO in treating cyclic mastalgia. Female patients diagnosed with cyclic mastalgia (N = 156; 25-45 years old) were randomly assigned to apply twice daily 2 g of NSO gel (a gel base combined with cold-pressed NSO; Barij Essence Pharmaceutical Co.; Kashan, Iran), 20 mg of topical diclofenac, or a placebo gel for two menstrual cycles. There were no significant differences in patient characteristics or baseline pain scores between groups. Pain scores in active treatment groups also did not differ significantly at cycles one and two. However, both active treatment groups experienced a significant decrease in pain scores by the end of the study compared to baseline and placebo. The authors


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*Nigella sativa*
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posited that thymoquinone, unsaturated fatty acids, and carvacrol may play a part in NSO's effectiveness for treating cyclic mastalgia. They also stated that the main shortcoming of the study was the lack of follow-up, which might have been helpful since recurrence of cyclic mastalgia is common.[71]

Two outcomes from a single RDBPC study were published in 2015 and 2016 on NSO and cardiovascular risk, and NSO and inflammation, respectively. Obese women (N = 84; 25-50 years old) took 3 g per day of cold-pressed NSO (Dana Co.; Tabriz, Iran) or placebo and followed a low-calorie diet for eight weeks. In the cardiovascular-risk arm of the study, the women in the NSO group experienced significant decreases compared to baseline in weight, waist circumference, and levels of triglycerides and very-low-density lipoprotein (VLDL). The authors suggested that NSO supplementation combined with a low-calorie diet may reduce cardiometabolic risk factors in obese women, but they noted that more studies are needed to assess the efficacy of NSO as a complementary therapy.[72] In the second arm of the study, NSO significantly decreased serum levels of TNF-α and high-sensitivity C-reactive protein compared to placebo. No significant changes were seen in IL-6 levels. Based on these findings, the authors concluded that NSO supplementation and calorie-restriction may modulate systemic inflammatory biomarkers in obese women but that more studies are needed to clarify the findings.[73]

A 2015 study assessed the effects of the previously mentioned NSO preparation on oxidative stress in obese women (N = 50; 25-50 years old). Investigators reported significant weight loss in the NSO group compared to the placebo group after eight weeks. Additionally, significant changes in superoxide dismutase (SOD, a natural antioxidant enzyme) occurred in the NSO group compared to the placebo group.[74]

Three studies of varying quality have been conducted on nigella for functional dyspepsia. In one RDBPC study, 70 patients diagnosed with functional dyspepsia took either a traditional formula consisting of 5 mL cold-pressed NSO, mineral oil, and honey (Barij Essence Pharmaceutical Co.; Kashan, Iran) or placebo daily for eight weeks. In both groups, significant decreases in dyspepsia severity scores as measured by the Hong Kong index of dyspepsia severity were seen in the second, fourth, and eighth weeks, but mean scores and the rate of *Helicobacter pylori* infection for the NSO group were significantly lower than in the placebo group at the end of the study. Additionally, there was a significant difference in quality of life between the NSO and placebo groups at eight weeks.[75]

A 2015 meta-analysis and systematic review assessed 17 randomized, controlled trials that examined the effects of *N. sativa* on plasma lipid concentrations. The authors suggested that there was a significant association between NS supplementation and reduction in total cholesterol and triglyceride levels. No significant effects were seen on high-density lipoprotein (HDL) cholesterol levels. NSO performed better than NS powder in lowering total serum cholesterol and low-density lipoprotein (LDL) cholesterol, but only NS powder was found to increase HDL cholesterol. The authors recommended that further randomized, controlled trials are needed to explore nigella's benefits for cardiovascular health.[76]

## FUTURE OUTLOOK

There are no known comprehensive reports available on the conservation status of wild *N. sativa* in its native habitat. However, it has been cultivated for thousands of years, and the commercial supply is not known to originate from wild populations. Historically, the main producers and exporters of cultivated *N. sativa* seed have been Egypt, Turkey, Syria,[18] and India.[12] Because *N. sativa* seed is widely used in the Indian systems of medicine, the plant is cultivated on a large scale and estimated to be traded in annual quantities in excess of 100 metric tons (MT).[20] Certified organic *N. sativa* seed comes predominantly from farms in Egypt and, to a lesser extent, Turkey.[10]

Market prices for cultivated *N. sativa* seed from the two main countries of origin, Egypt and India, have generally been stable. In late 2016, prices for full container load (FCL) quantities of conventional *N. sativa* seed from India ranged from $2,258 to $2,750 per MT (Free on Board [FOB]* Mumbai Port). Conventional Egyptian material sold for $2,900 per MT (FOB Alexandria Port). Some Egyptian exporters were also offering FCL quantities of fair trade and certified organic *N. sativa* seed for $3,000 per MT (FOB Alexandria Port).[77]

The quantities of seed needed for use in the various traditional African and Asian systems of medicine, as well as for culinary use, are already considerable, and due to the significant levels of promising new clinical research, it seems likely that production and demand will increase, especially for value-added forms, such as oils and extracts. HG

**—Gayle Engels and Josef Brinckmann**

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* Free On Board means that the price only includes the cost of the item. Seller arranges for transport of the goods, preparing goods for shipment, and loading the goods onto the vessel.






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# American Botanical Council Presents Annual Botanical Excellence Awards

**The American Botanical Council (ABC) hosted its 12th annual American Botanical Celebration and Awards ceremony on March 9, 2017, at the Hilton Anaheim in Anaheim, California, in conjunction with the Natural Products Expo West trade show. This popular event celebrated outstanding contributions to the herbal community with the presentation of the prestigious ABC Botanical Excellence Awards. The event also provided a unique opportunity to acknowledge the much-appreciated support of ABC Sponsor Members.**

At the celebration, approximately 350 guests came together to support ABC. Attendees included ABC Sponsor Members, members of the ABC Board of Trustees, Advisory Board, and Director's Circle, and many others. The evening, which was filled with intriguing conversations, vegetarian hors d'oeuvres, and a wide variety of cocktails, was capped off with a short ceremony during which the Excellence Awards were presented.

Medicinal plant expert Josef Brinckmann was named the third recipient of the ABC Champion Award. ABC Founder and Executive Director Mark Blumenthal introduced Brinckmann, who spoke about his love of herbs and medicinal plants, their sustainability, and the fact that his extensive volunteer work for ABC's unique nonprofit educational mission does not seem like "work" to him since he loves herbs so passionately.

The Varro E. Tyler Commercial Investment in Phytomedicinal Research Award was presented by ABC Chief Science Officer Stefan Gafner, PhD, to Brassica Protection Products, a phytomedicine company based in Baltimore, Maryland. CEO Tony Talalay accepted the award on behalf of the company.

For the second consecutive year, the James A. Duke Excellence in Botanical Literature Award was presented to a book focused on aromatherapy: *Handbook of Essential Oils: Science, Technology, and Applications*, 2nd edition, edited by K. Hüsnü Can Başer, PhD, and Gerhard Buchbauer, PhD. The award was accepted by Başer's son, Bala.

The Norman R. Farnsworth Excellence in Botanical Research Award was presented to Her Excellency Ameenah Gurib-Fakim, PhD, President of the Republic of Mauritius. Gurib-Fakim accepted the award via a pre-recorded video.

The fifth annual Mark Blumenthal Herbal Community Builder Award was announced to the group assembled at the ABC Celebration and was presented by Blumenthal to Ikhlas Khan, PhD, the director of the National Center for Natural Products Research (NCNPR) at the University of Mississippi (UM), at the annual International Conference on the Science of Botanicals (ICSB) at UM on April 4.

## *Handbook of Essential Oils* Receives Duke Award for Excellence in Botanical Literature Award

The Duke Award was created in 2006 to honor economic botanist and author James A. Duke, PhD. Along with his many prestigious career achievements in economic botany and ethnobotany and decades of work at the United States Department of Agriculture, Duke has authored more than 30 reference and consumer books. He is also a co-founding member of ABC's Board of Trustees and currently serves as director emeritus. ABC gives the award annually to books that contribute significantly to the medicinal plant-related literature, and the fields of botany, taxonomy, ethnobotany, phytomedicine, and other disciplines.

ABC previously recognized essential oils and their clinical applications with the 2015 award to *Clinical Aromatherapy: Essential Oils in Healthcare*, 3rd edition. Başer and Buchbauer's *Handbook of Essential Oils* offers a different contribution to the literature by providing a greater scientific understanding of the production, chemistry, pharmacology, toxicology, and other relevant aspects of essential oils.





Mark Blumenthal, ABC founder and executive director, addresses the crowd at the 12th annual American Botanical Celebration ceremony.

"Essential oils are one of the fastest growing segments of the herbal product market," noted Blumenthal. "Last year, we bestowed the Duke Award to Dr. Jane Buckle for her excellent book, which documents the evidence-based data for the safe and effective therapeutic uses of many essential oils. This year, we recognize another excellent reference book that provides much of the chemical, quality control, pharmacological, and toxicological bases supporting many of these therapeutic uses."

Başer is a professor of pharmacognosy at the Near East University in Northern Cyprus, and Buchbauer is the head of the Department of Clinical Pharmacy and Diagnostics at the University of Vienna in Austria. "I am deeply grateful to Mark Blumenthal and the selection committee for bestowing upon my colleague and me this highly prestigious award," wrote Başer. "The current and future research into essential oils and their volatile constituents is expected to lead to a better understanding and discovery of potential new uses of these valuable natural products."

Buchbauer also expressed his gratitude for the award. "We are very pleased about the acknowledgment of our efforts to further develop the science of essential oils," he wrote. "The goal to provide a strong scientific basis for essential oils was and is our everlasting concern."

Gafner congratulated the authors, noting that "with its broad coverage of aromatic plant agriculture, essential oil manufacturing, quality control, and medicinal and culinary uses, this book has become *the* reference on essential oils in the cosmetic industry and beyond."

Past Duke Award recipients include: *Clinical Aromatherapy*, 3rd edition (2015); *Ancient Pathways, Ancestral Knowledge* (2014); *Principles and Practice of Phytotherapy*, 2nd edition (2013); *Medicinal Plants and the Legacy of Richard E. Schultes* (2012; reference/technical category) and *Smoke Signals* (2012; consumer/popular category); *Healing Spices* (2011; consumer/popular category) and the American Herbal Pharmacopoeia's *Botanical Pharmacognosy* (2011; reference/technical category); *Botanical Medicine for Women's Health* (2010); *An Oak Spring Herbaria* (2009); and *Mabberley's Plant-Book*, 3rd edition (2008).

## President of Republic of Mauritius Recognized for Outstanding Contributions to Medicinal Plant Research

Gurib-Fakim leads her country as an advocate for African medicinal plants, and has made valuable contributions to the knowledge of the medicinal properties of plants growing on Mauritius and the surrounding islands in the Indian Ocean.

ABC presents the annual award, named in honor of celebrated professor Norman R. Farnsworth, PhD, to an individual who has made significant contribu-


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tions to research in the fields of ethnopharmacology and/or other areas of medicinal plant research. Farnsworth, who died in 2011, was one of the co-founding members of ABC's Board of Trustees, a highly published and internationally renowned research professor of pharmacognosy, and a senior university scholar in the College of Pharmacy at the University of Illinois at Chicago.



Her Excellency Ameenah Gurib-Fakim, President of the Republic of Mauritius, sent a video acceptance speech for the ABC 2016 Norman R. Farnsworth Excellence in Botanical Research Award.

Blumenthal praised Gurib-Fakim's "extraordinary" achievements. "ABC is deeply honored to be able to recognize the excellent ethnobotanical, pharmacognostic, and conservation efforts and publications of Her Excellency Dr. Ameenah Gurib-Fakim," he said. "Her tireless work on medicinal plants in the Indian Ocean and East African region has already garnered several well-deserved and high-profile international awards. I am certain that the late Professor Farnsworth would approve of ABC's selection of Dr. Gurib-Fakim to receive his eponymous award."

Gurib-Fakim was elected as Mauritius's first female president in 2015. Prior to her election, she worked as managing director of Centre International de Développement Pharmaceutique (CIDP) Research and Innovation, where she researched the indigenous medicinal plants of Mauritius. Her research interests include ethnobotany and ethnomedicine, and the bioactivity, chemical composition, and quality control of medicinal plants, particularly those with antimicrobial properties. She has authored or co-authored more than 100 research publications and dozens of books, including *An Illustrated Guide to the Flora of Mauritius and the Indian Ocean Islands*, a three-volume compilation of *The Medicinal Plants of Mauritius*, *Chemistry for Sustainable Development in Africa*, and the *African Herbal Pharmacopoeia*.

"Biodiversity and indigenous knowledge systems underpin life on earth," said Gurib-Fakim. "Africa's unique biodiversity will continue to offer humankind new leads and medicine provided that we conserve, document, and validate the traditional knowledge associated with medicinal plants. The latter remains a reservoir of innovative ingredients that not only respond to the needs of industry but also buffer us against ailments that do not yet exist."

Gafner commented: "Research on the medicinal properties of plants from the African continent is certainly close to my heart, since this was the topic of my graduate research. Therefore, I am very pleased that this year's award goes to Her Excellency Dr. Gurib-Fakim. Her work on the chemistry, bioactivity, and medical uses of medicinal plants of Africa and the Indian Ocean represents the very essence of what this award intends to recognize: an exceptional career in pharmacognosy research."

Past recipients of the Farnsworth award include: John T. Arnason, PhD (2015); Harry Fong, PhD (2014); Gordon Cragg, PhD (2013); De-An Guo, PhD (2012); Djaja Soejarto, PhD (2011); A. Douglas Kinghorn, PhD (2010); Rudolf Bauer, PhD (2009); Ikhlas Khan, PhD (2008); Hildebert Wagner, PhD (2007); Edzard Ernst, MD, PhD (2006); and Joseph Betz, PhD (2005).

## Brassica Protection Products Receives Tyler Award for Phytomedicinal Research

Since its founding in 1997, Brassica Protection Products has been dedicated to the research and development of beneficial phytochemicals from cruciferous vegetables in the genus *Brassica*.

The ABC Tyler Award was created to honor one of the most respected scientists in late-20th century herbal medicine and pharmacognosy. Tyler was an early trustee of ABC, and vice president of academic affairs and dean of the College of Pharmacy and Pharmaceutical Sciences at Purdue University. He was the senior author of six editions of a leading pharmacognosy textbook, and numerous other professional and popular books and academic articles. Tyler encouraged scientific and product integrity, and envisioned a rational phytomedicinal health care sector that valued the proper evaluation of products' quality, safety, and efficacy.




Tony Talalay (center) of Brassica Protection Products accepts the ABC Tyler Award for Phytomedicinal Research.

Through partnership with the Johns Hopkins School of Medicine, Brassica Protection Products has laid the foundation for understanding the medicinal properties of broccoli. Paul Talalay, MD, Distinguished Service Professor of Pharmacology and Molecular Sciences at Johns Hopkins, was an early proponent of cancer prevention through the intake of specific diet-derived vegetable compounds. He discovered the ability of sulforaphane, a compound produced by cruciferous vegetables, to induce the production of enzymes that help eliminate toxic metabolites from the body. It was proposed that this was one of the mechanisms by which broccoli exerts its cancer-preventive activity.

"Being honored with the ABC's prestigious Varro E. Tyler Award is a wonderful tribute to a lifetime of research by my father, Paul Talalay, who has dedicated himself to understanding the body's own protective systems and elucidating the benefits of broccoli, glucoraphanin, and sulforaphane in promoting human health," said Talalay. "This award is a confirmation of Brassica's mission to bring scientifically valid nutritional products to consumers. It is especially gratifying as it recognizes the company's primary goal — to continually ensure quality commercialization efforts that honor the extraordinary quality of the science."

After a number of additional studies evaluated the properties of broccoli extracts in vitro and in animals, Paul Talalay founded Brassica Protection Products with his colleague Jed Fahey, ScD. One year later, they published findings on the human metabolism and elimination of sulforaphane and other sulfur-containing compounds found in cruciferous vegetables, which paved the way for subsequent clinical studies. Paul Talalay and Fahey have published about half a dozen clinical trials that have investigated the effects of broccoli extracts. These trials have shown the ability of broccoli extracts to attenuate gastritis by reducing the colonization of *Helicobacter pylori* bacteria, and by reducing the time it takes to eliminate airborne pollutants from the body.

Blumenthal noted: "ABC previously granted the Varro E. Tyler Award to companies that committed to funding clinical research on their proprietary ingredients or products. This year we are recognizing the enormously significant and pioneering research of Paul Talalay in the area of human nutrition, particularly on phytochemicals in plants in the family Brassicaceae for the prevention of certain cancers."

Previous recipients of the ABC Tyler Award include MediHerb/Integria Healthcare (2015); SFI Flordis International (2014); Wakunaga Pharmaceutical Company (2013); Horphag Research (2012); Bioforce AG (2011); New Chapter (2010); Bionorica AG (2009); Indena SpA (2008); and Dr. Willmar Schwabe Pharmaceuticals (2007).

## Medicinal Plant Expert Josef Brinckmann Receives ABC Champion Award

The ABC Champion Award was created to recognize individuals who have been outstanding supporters of ABC and have helped the organization promote and achieve its nonprofit educational mission. The generosity of ABC's friends and members is vital to the nonprofit's continued success and growth.

"While those of us working in the field are not carrying out the work in hopes of an eventual award, I am deeply appreciative that my life's work for the sustainable harvesting and rational use of medicinal plants is being recognized by the American Botanical Council," wrote Brinckmann. "I am genuinely grateful for the opportunities given to me over the years to research and write about the plants in support of ABC's educational mission."




Josef Brinckmann accepts the ABC Champion Award.

Since 1979, Brinckmann has worked for the Sebastopol, California-based medicinal tea company Traditional Medicinals. He joined the company as manager of operations and purchasing, and later served as vice president of research and development and vice president of sustainability. In 2016, Brinckmann became a research fellow for medicinal plants and the botanical supply chain.

Brinckmann is a frequent contributor to ABC publications, particularly the quarterly peer-reviewed journal *HerbalGram*. Beginning with issue 90 in 2011, he has co-authored more than 20 herb profiles with ABC Special Projects Director Gayle Engels. Brinckmann has also written numerous feature articles, including the cover story of issue 75 on Peruvian maca and a feature in issue 90 on quality standards for botanical ingredients. Additionally, he has served as a peer reviewer for dozens of articles in ABC publications.

"This award could not go to a better recipient. Josef is a true champion of the plants," said Engels. "I wish that all of ABC's constituents were aware of how tremendously beneficial his participation is to ABC and its educational mission. I am in awe of his breadth of knowledge and commitment to quality and am honored to have worked with him over the years."

Blumenthal also praised Brinckmann's significant and ongoing contributions to ABC. "Previous recipients of this award — my good friends Terry Lemerond and Ed Smith — were acknowledged for their generous donations to ABC to support our unique nonprofit research and educational mission, publications, and programs," he said. "This year we acknowledge Josef Brinckmann for investing an immense amount of his personal time and energy in providing ABC with his extensive knowledge and global experience to support ABC's numerous educational publications and programs."

In addition to his work at Traditional Medicinals, Brinckmann is an international consultant on medicinal plants market intelligence for the International Trade Centre, a founding member of the FairWild Foundation's board of trustees, a member of the United States Pharmacopeia's expert committee on botanical dietary supplements and herbal medicines, and an ABC Advisory Board member.

In 2016, Brinckmann was granted an honorary doctorate by the California Institute for Integral Studies for his highly valued and appreciated global work in sustainability of medicinal and aromatic plants.

Previous recipients of the ABC Champion Award include Ed Smith (2015), medical herbalist and co-founder of Herb Pharm, and Terry Lemerond (2014), founder of EuroPharma, Inc. and Enzymatic Therapy.

## Ikhlas Khan Receives 2016 ABC Mark Blumenthal Community Builder Award

This annual award is given to an individual who has played a significant role in creating a sense of community among herbalists, researchers, members of the herb and natural products communities, and related individuals who work in the area of medicinal plants.

"I am honored to receive this recognition — this award named after Mark Blumenthal, who is a living example of a community builder," said Khan.

Blumenthal said that "through organizing the International Conference on the Science of Botanicals (ICSB) for 17 years, in partnership with the US Food and Drug Administration (FDA), Professor Ikhlas Khan has created a global community of researchers, regulators, and others who have an interest in furthering the appropriate production and responsible use of scientifically supported medicinal plants products."

On January 1, 2017, Khan became the director of the NCNPR at UM in Oxford, Mississippi, following the retirement of former director Larry Walker, PhD. Previously, Khan had been the associate director of the NCNPR. The NCNPR is part of UM's Research Institute of Pharmaceutical Sciences (RIPS) and is a primary partner with ABC and the American Herbal Pharmacopoeia (AHP) in the ABC-AHP-NCNPR Botanical Adulterants Program.




Ikhlas Khan accepts the ABC Mark Blumenthal Herbal Community Builder Award at the ICSB at UM on April 4, 2017.

Khan's primary research interests include drug discovery from medicinal plants and the development of reference standards and laboratory analytical methods for botanical identity, purity, and safety. He is a research professor of pharmacognosy at UM.

In addition, Khan, who was born in Amroha, India, is the director of the Sino-US Traditional Chinese Medicine Research Center, director of the Center for Research of Indian Systems of Medicine, and coordinator of NCNPR efforts at the Center for Water and Wetlands Resources, which are all at UM.

Khan received a bachelor's degree in chemistry and a master's degree in organic chemistry from Aligarh Muslim University in Aligarh, India. In 1987, he received a doctorate in pharmacy from the Institute for Pharmaceutical Biology in Munich, Germany, where he studied under internationally renowned medicinal plant research expert Hildebert Wagner, PhD. In 1988, he joined RIPS at UM as a postdoctoral research associate. In 1990, he received a postdoctoral position with the Department of Pharmacy at the Swiss Federal Institute of Technology in Zurich, Switzerland. In 1992, he was appointed as a research scientist at UM.

He has authored or co-authored more than 700 research articles and has been a co-editor of the highly regarded research journal *Planta Medica* and a foreign editor of the *Journal of Traditional Chinese Medicine*.

Khan also served on a committee for the National Center for Complementary and Integrative Health at the US National Institutes of Health, an expert panel for the United States Pharmacopeia, an expert advisory committee of the Natural Products Health Directorate of Health Canada, and the Advisory Board of ABC.

He co-directs the NCNPR's medical cannabis farm, which supplies high-quality medical cannabis and its constituents to the National Institute on Drug Abuse Drug Supply Program, which then distributes the materials to medical marijuana researchers under contract.

Khan, who speaks four languages (English, German, Hindi, and Urdu), has been the recipient of numerous awards for his scientific achievements, including the American Society of Pharmacognosy's Tyler Prize in 2011, the American Herbal Products Association's Herbal Insight Award in 2010, the FDA's Commissioner's Special Citation in 2009, and ABC's Norman R. Farnsworth Excellence in Botanical Research Award in 2009.

Past recipients of ABC's Community Builder Award include herbalist and co-founder of the American Herbalists Guild Michael Tierra (2015), president of the United Natural Products Alliance Loren Israelsen (2014), Herb Pharm co-founder Sara Katz (2013), and herbalist and author Rosemary Gladstar (2012). HG

**—ABC Staff**

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# EuroPharma Supports ABC's Educational Mission through Turmeric Adoption

**The American Botanical Council (ABC) welcomes EuroPharma to the growing list of Adopt-an-Herb supporters though its adoption of turmeric (*Curcuma longa*, Zingiberaceae). By adopting turmeric, EuroPharma helps ABC expand its nonprofit educational mission and keep its unique HerbMedPro database updated with the latest scientific and clinical research on this popular medicinal plant.**

HerbMedPro is a comprehensive, interactive online database that provides access to important scientific and clinical research data on the uses and health effects of approximately 250 herbs.

ABC Founder and Executive Director Mark Blumenthal said: "All of us at ABC are deeply grateful to Terry Lemerond, Cheryl Myers, Lisa Joski, and the entire EuroPharma team for its adoption of turmeric, one of the most popular herbs in today's market. There is so much scientific and clinical information being published each year on turmeric rhizome and its extracts — a veritable explosion of research findings — that it is quite challenging to keep up with reading and summarizing the literally hundreds of new papers cited in our robust HerbMedPro database."

EuroPharma's founder Terry Lemerond praised the Adopt-an-Herb initiative, and said: "Representing turmeric, an herb with such life-changing possibilities and significant clinical studies in the evidence-based database of ABC, is a great alignment with the mission of EuroPharma. We look forward to stewarding the ever-growing scientific and clinical data on this far-reaching herb, which contains the key component curcumin: a compound with an extraordinary scientific profile."

## About Turmeric

The turmeric rhizome has a long history of use in Ayurveda, India's oldest system of traditional medicine, and in traditional Chinese medicine. Traditionally, turmeric was used internally for indigestion and topically for skin sores and wounds. Many commercially available turmeric extracts are standardized to the level of curcuminoids, a group of biologically active phytochemicals in turmeric, which are collectively known in the marketplace as "curcumin." The anti-inflammatory actions of curcumin may play a large role in its potential therapeutic benefits. Turmeric and curcumin are being investigated in research trials for their ability to treat a range of health conditions, such as depression and cognitive decline, and as potential adjunct agents in certain types of cancer.

## About EuroPharma

For more than 35 years, EuroPharma has provided the United States with lab-tested natural medicines and proprietary formulations. EuroPharma was founded by Lemerond, who has more than 40 years of experience in the health food industry and received ABC's first Champion Award in 2015. In 2017, Lemerond was inducted into the New Hope Hall of Legends at Natural Products Expo West. EuroPharma's Curamin formulas use clinically studied ingredients, including BCM-95 curcumin extract, for a variety of health benefits.

## About Adopt-an-Herb and HerbMedPro

EuroPharma is one of 44 companies that have supported ABC's educational efforts to collect, organize, 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, a total of 51 herbs have been adopted.

Each adopted herb is continuously researched for new articles and studies, which ensures that its HerbMedPro record stays current and robust. The result is an unparalleled resource not only for researchers, health professionals, industry, and consumers, but also for members of the herbal and dietary supplements community.

HerbMedPro is available to ABC members at the Academic level and higher. Its "sister" site, HerbMed, is free and available to the general public. In keeping with the ABC's position as an independent research and education organization, herb adopters do not influence the scientific information that is compiled for their respective adopted herbs. HG

**—ABC Staff**




**Turmeric** *Curcuma longa*
Photo ©2017 Steven Foster





# ABC's Blumenthal Receives 'Outstanding International Ethnopharmacologist of the Year' Award

**The Society for Ethnopharmacology-India (SFE-India) has presented its "SFE – Outstanding International Ethnopharmacologist Award – 2017" to Mark Blumenthal, founder and executive director of the nonprofit American Botanical Council (ABC). The award was given to Blumenthal at the society's annual meeting and scientific conference in Surat, Gujarat, India, on February 23, 2017.**

Ethnopharmacology is a branch of pharmacology that focuses on the knowledge and customs concerning medicinal substances, especially those of plant origin, and their use in traditional medicine. Ethnopharmacology pertains not only to traditional ethnobotany, but also to the modern scientific and clinical research on the safety and activity of historically used medicinal substances. It also involves quality control of these substances since they are used in modern societies (e.g., as foods, dietary supplements, and medicines).

"SFE-India is happy to confer the 'SFE – Outstanding International Ethnopharmacologist Award – 2017' to Mark Blumenthal for his outstanding contributions to the fields of ethnobotany, ethnopharmacology, and medicinal plant research," wrote Pulok Mukherjee, PhD, secretary of SFE and director of the School of Natural Product Studies at Jadavpur University in Kolkata, India.

Blumenthal has more than 45 years of experience in the fields of herb and medicinal plant education, research, publishing, quality control, regulation, market dynamics, and related areas. He has served as the executive director of ABC since he founded the organization in 1988, and he also serves as editor-in-chief of the nonprofit's peer-reviewed journal *HerbalGram,* which he launched in 1983. In addition, Blumenthal is the senior editor of three highly regarded reference books on medicinal plants and co-editor of two additional reference books. He is also editor-in-chief of ABC's HerbClip series of summaries and critical reviews of clinical studies and other scientific publications on herbs, medicinal plants, phytomedicines, teas, essential oils, plant-based foods, and fungi.

As the founder and director of the ABC-AHP-NCNPR Botanical Adulterants Program, Blumenthal has been active in the international herb community in the areas of quality control and adulteration of botanical raw materials and extracts. The program is an international effort that has been underwritten or endorsed by more than 180 responsible parties, including manufacturers of medicinal plant products, trade associations, societies of researchers and health professionals, analytical laboratories, university research centers, and other stakeholders. It is a partnership among ABC, the nonprofit American Herbal Pharmacopoeia (AHP), and the University of Mississippi's National Center for Natural Products Research (NCNPR), which is a US Food and Drug Administration Center for Excellence for the analysis of botanical ingredients used in dietary supplements.

"I am deeply honored and grateful to receive this award, which recognizes the international impact of the educational efforts of the American Botanical Council," said Blumenthal in his acceptance of the award. "With members in more than 80 countries, ABC is truly an international organization."

"Medicinal plant research and quality control are international; they are not limited by political borders," he continued. "Scientists share their information globally for the highest benefit to all humankind, and I am pleased that ABC's educational publications and programs are valued by our professional colleagues in India, a country with a rich history and tradition of medicinal plant use and robust modern scientific research."

ABC Chief Science Officer Stefan Gafner, PhD, added: "Mark Blumenthal has a lifelong commitment to promote the responsible use of medicinal plants. The traditional use of medicinal plants by various cultures has always been one of his prime interests. Examples include the ABC-organized ecotours for pharmacists to learn about the 'pharmacy of the rainforest' in Peru, Belize, Costa Rica, and parts of Africa. Mark is only the fourth recipient of this prestigious award, and I congratulate him for this well-deserved recognition of his contributions to the field of ethnopharmacology."

Previous recipients of the award include Michael Heinrich, PhD, professor of pharmacognosy at the University College London; Geoffrey Cordell, PhD, retired professor emeritus of pharmacognosy at the University of Illinois-Chicago; and Robert Verpoorte, PhD, professor emeritus at Leiden University.

## About SFE-India

The Society for Ethnopharmacology-India, which is composed of academicians, researchers, and members of the industry, works to disseminate knowledge for the promotion of ethnopharmacology and medicinal plants. In keeping with its mission of "Globalizing local knowledge and localizing global technologies," SFE-India strives to provide an environment for knowledge-sharing among researchers, health care practitioners, and decision-makers who are interested in promoting ethnopharmacology and medicinal plants. HG

**—ABC Staff**

# Botanical Adulterants Bulletin Highlights the Presence of Synthetic Antimicrobial Compounds in 'Grapefruit Seed Extract'

**The American Botanical Council (ABC)-American Herbal Pharmacopoeia (AHP)-National Center for Natural Products Research (NCNPR) Botanical Adulterants Program (BAP) has published a new Botanical Adulterants Bulletin (BAB) on the adulteration of grapefruit seed extract (GFSE).**

GFSE is marketed as a dietary supplement with antimicrobial activity and as a natural preservative for personal care and cosmetic products. The seed of grapefruit (*Citrus paradisi*, Rutaceae) has no known history of use in traditional herbal medicine.

As early as 1991, the occurrence of undeclared synthetic antimicrobial compounds (i.e., triclosan and methylparaben) was reported in products marketed as GFSE. Thirteen published papers have provided evidence for adulteration of GFSE with these and other synthetic microbicides, such as benzalkonium chloride, benzethonium chloride, cetrimonium bromide, and propylparaben. However, none of these studies found chemical compounds that are characteristic of grapefruit seed in the adulterated products, which suggests that any antimicrobial effects of these products were due to the undeclared microbicides rather than authentic GFSE.

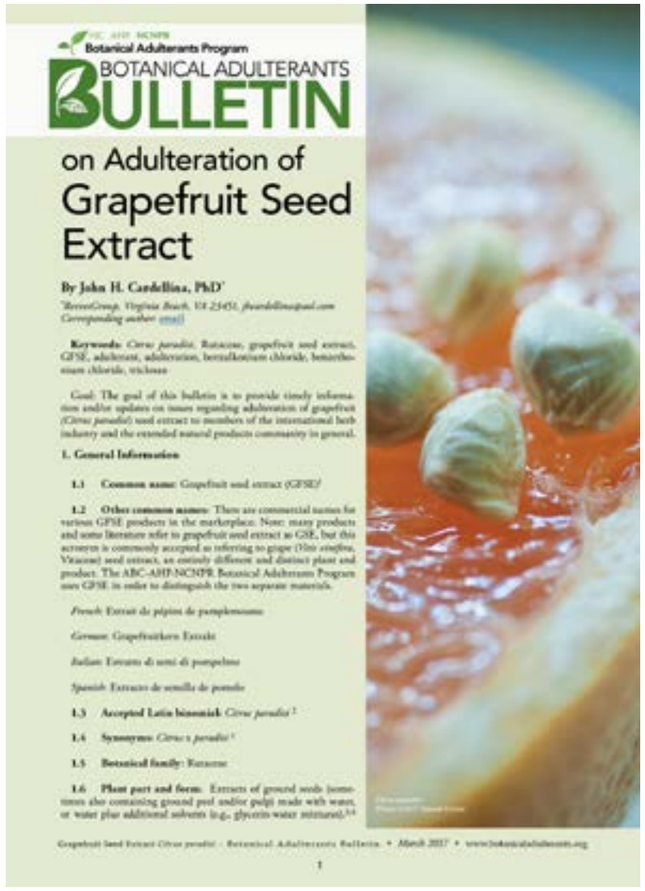
The GFSE bulletin contains information about the production and market importance of GFSE, known adulterants, and analytical approaches to detect adulterants. It was authored by John Cardellina, PhD, chief technical consultant and associate editor of BAP. The bulletin has been peer reviewed by 12 experts from contract analytical laboratories, nonprofit organizations, the US government, and the herb and dietary supplement industry.

The goal of the BABs is to provide accounts of ongoing issues related to botanical identity and adulteration and inform quality control personnel and lab technicians in the herbal medicine, dietary supplement, cosmetic, conventional food, and other industries in which botanical ingredients are used about adulteration problems that may be widespread and/or that may constitute safety problems.

This bulletin marks the second publication on GFSE as part of the BAP's ongoing efforts to educate industry members and other stakeholders about the adulteration of GFSE. The first publication on GFSE adulteration appeared in issue 94 of ABC's peer-reviewed journal *HerbalGram* in 2012.

"The adulteration of 'grapefruit seed extract' with undisclosed synthetic disinfectant chemicals is a particularly egregious practice," noted Mark Blumenthal, founder and executive director of ABC and director of the BAP. "There has been no credible explanation as to why these synthetic compounds have been continually detected by independent laboratories over the past 25 years; the only logical conclusion is that they are being added intentionally. This appears to be adulteration, and, as such, it is fraud. This issue requires investigation by the US Food and Drug Administration and other appropriate agencies internationally."

Cardellina commented: "Almost five years after publication of the review of the adulteration of GFSE in *HerbalGram*, analyses continue to show that some so-called GFSE products in the marketplace are adulterated with synthetic microbicides. A recent seminal paper from the research group of Ikhlas Khan, PhD, at the NCNPR at the University of Mississippi provides a critical new tool to address this problem: an analytical method that can simultaneously identify and quantify both the natural constituents of grapefruit seed and also the suite of synthetic disinfectants found for more than 25 years in commercial GFSE products. This new method warranted the issuance of this bulletin."


Botanical Adulterants Program

BOTANICAL ADULTERANTS BULLETIN

on Adulteration of Grapefruit Seed Extract

By John H. Cardellina, PhD†

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**Keywords:** *Citrus paradisi*, Rutaceae, grapefruit seed extract, GFSE, adulterant, adulteration, benzalkonium chloride, benzethonium chloride, triclosan

Goal: The goal of this bulletin is to provide timely information and/or updates on issues regarding adulteration of grapefruit (*Citrus paradisi*) seed extract to members of the international herb industry and the extended natural products community in general.

**1. General Information**

**1.1 Common name:** Grapefruit seed extract (GFSE)[1]

**1.2 Other common names:** There are commercial names for various GFSE products in the marketplace. Note: many products and some literature refer to grapefruit seed extract as GSE, but this acronym is commonly accepted as referring to grape (*Vitis vinifera*, Vitaceae) seed extract, an entirely different and distinct plant and product. The ABC-AHP-NCNPR Botanical Adulterants Program uses GFSE in order to distinguish the two separate materials.

*French:* Extrait de pépins de pamplemousse

*German:* Grapefruitkern Extrakt

*Italian:* Estratto di semi di pompelmo

*Spanish:* Extracto de semilla de pomelo

**1.3 Accepted Latin binomial:** *Citrus paradisi*[2]

**1.4 Synonyms:** *Citrus x paradisi*[3]

**1.5 Botanical family:** Rutaceae

**1.6 Plant part and form:** Extracts of ground seeds (sometimes also containing ground peel and/or pulp) made with water, or water plus additional solvents (e.g., glycerin-water mixtures).[3,4]

Grapefruit Seed Extract *Citrus paradisi* – Botanical Adulterants Bulletin • March 2017 • www.botanicaladulterants.org

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The ABC-AHP-NCNPR Botanical Adulterants Program is an international consortium of nonprofit professional organizations, analytical laboratories, research centers, industry trade associations, industry members, and other parties with interest in herbs and medicinal plants. The program advises industry, researchers, health professionals, government agencies, the media, and the public about the various challenges related to adulterated botanical ingredients sold in commerce. To date, more than 180 US and international parties have financially supported or otherwise endorsed the program.

The GFSE bulletin is the ninth publication in the series of BABs. As with all publications in the program, the bulletins are freely accessible on the program's website.

## About the Botanical Adulterants Program

In the coming months, the program plans to release additional bulletins on ashwagandha (*Withania somnifera*, Solanaceae) root, rhodiola (*Rhodiola rosea*, Crassulaceae) root and rhizome, and tea tree (*Melaleuca alternifolia*, Myrtaceae) oil.

To date, the BAP has published seven extensively peer-reviewed articles on the history of adulteration, the adulteration of the herbs black cohosh (*Actaea racemosa*, Ranunculaceae) and skullcap (*Scutellaria lateriflora*, Lamiaceae), adulteration of bilberry (*Vaccinium myrtillus*, Ericaceae) fruit extract and pomegranate (*Punica granatum*, Lythraceae) fruit products, the history of ginseng (*Panax* spp., Araliaceae) taxonomy, nomenclature, and trade as a basis for understanding ginseng adulteration, and the sale of synthetic antimicrobial compounds labeled to contain GFSE.

In addition, the program has published four Laboratory Guidance Documents (LGDs) that review and evaluate analytical methods to authenticate and detect adulteration of bilberry extract, black cohosh, and skullcap. The fourth LGD, on GFSE, was published in May. The program also publishes a quarterly e-newsletter, the Botanical Adulterants Monitor, that highlights new scientific publications related to botanical authenticity and analysis to detect possible adulteration, recent regulatory actions, and program news. All of the program's publications are freely available on the ABC website, www.herbalgram.org. HG

**—ABC Staff**

Botanical Adulterants Program

**Grapefruit** *Citrus paradisi*
Photo ©2017 Steven Foster



# Supplement Online Wellness Library Launched in April

**In April, the Supplement Online Wellness Library (OWL; www.SupplementOWL.org), an industry-wide dietary supplement product registry, became accessible to the public for the first time. The registry, which began accepting label submissions in November 2016, is a self-regulatory initiative spearheaded by the Council for Responsible Nutrition (CRN), a leading dietary supplement industry association, and developed in partnership with Underwriters Laboratories (UL), a global independent safety science company. Though it is considered primarily a tool for the dietary supplements industry, the Supplement OWL has begun to receive broad support from the natural products community, including endorsements by the American Botanical Council (ABC), Natural Products Association, and Consumer Healthcare Products Association. The registry will promote transparency in the manufacturing process, and regulators and retailers can use it see what ingredients are in the marketplace and who provides them.**

The voluntary two-tiered registry provides a central location for labels of dietary supplement products. Tier 1 is free and includes images of supplement labels and information about the products' ingredients, servings, and allergens. Companies also submit contact information for the product's manufacturing and packaging facility that will be accessible only to the US Food and Drug Administration. Each product in the registry is assigned a unique identifier number.[1]

Some of these functions, such as allowing retailers to look at a product's certifications or scientific substantiation, will come in the second phase of development, which is currently underway. Tier 2 of the program will provide benchmarks for understanding quality measures and a centralized location for maintaining and sharing information. "We aren't a regulatory agency. We have no guns and badges, and we can't stop non-compliance, but we feel transparency is valuable to avoid the activity of non-compliant players," said Duffy MacKay, ND, CRN's vice president of scientific and regulatory affairs (oral communication, March 27, 2017).

Tier 2, which does require the company to pay a fee, was designed so companies can upload quality and safety information and share it with customers as they choose. "We have heard loud and clear from retailers that they want more tools to understand industry and the activities in place to ensure compliance," MacKay added.

According to CRN and UL, the program has gained significant momentum in recent months. However, the number of products registered in the database is still representative of the early stage of the project, MacKay said. The exact number of registered products is difficult to pin down, said Erik Eberhart, UL's global development marketing manager for food, beverage, and nutrition (oral communication, April 3, 2017). "There has been a last-minute rush of people wanting to participate, so we are excited about that response and support," he said.

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## A Potential Domino Effect

As the database debuts, MacKay noted that CRN is eager to see the effect when companies not in the registry notice that leading players are embracing it. The hope is that this will pull along those in the middle and smaller sectors that may not see it as a priority. "These bigger companies were around for passage of DSHEA [the Dietary Supplement Health and Education Act of 1994], the promulgation of GMPs [good manufacturing practices], and supported mandatory serious adverse events reporting," he said. "They have seen the positive impact of these measures, which helped us to position our products as health promoting and responsibly made."

The OWL database represents a multi-year effort in which the industry came together to increase transparency in the industry, but it has been a long time coming. The concept first came up years earlier as retailers began requiring their vendors to register products in the US National Institutes of Health's (NIH's) Office of Dietary Supplements (ODS) label database,[2] and once in a bill sponsored by Senator Richard Durbin (D-Ill). (The bill, S. 1425, introduced August 1, 2013, amended the Federal Food, Drug and Cosmetic Act to expand registration requirements for dietary supplements.[2]) After the Durbin bill failed, MacKay recalled, "we realized [the proposed registry] was not that far-fetched and could be a reasonable addition to our regulatory cache."

The idea was gaining traction in wider industry leadership circles when the actions of the New York attorney general heightened the sense of urgency in February 2015. Realizing the importance of industrywide buy-in, CRN worked with non-members and other industry associations to shape the idea. It then engaged UL as a third-party administrator so that the whole industry would feel comfortable with the registry as an appropriate way to show commitment to transparency and help regulatory partners better understand industry products.

Companies like GNC, Herbalife, and Pharmavite were early influencers, and they urged colleagues and competitors to seize the opportunity.[3] There were also plenty of objections in the early phases of development. Some companies expressed concern about regulators using the database as a tool to scrutinize less than perfect manufacturing, processing, and labeling practices, MacKay explained (email, April 7, 2017). "If you are trying to hide something, then this is not the greatest idea," he said. "But the industry is maturing, and the majority of companies are now operating under the premise that compliance with regulations is the minimum action needed to make dietary supplements, and they want to show additional efforts being made toward ensuring product quality to the world."

Nine companies served as beta-testers and worked with UL to improve the process. The beta-testers, for example, helped UL identify challenges unique to the supplements industry and provided feedback on early versions of the database, Eberhart said. Adapting the program to upload different label formats was one of those challenges, and the UL team worked to capture and record information that might be in multiple places. "What came out of the first beta test is the ability to search on an ingredient level, find specific information that might be available in different places, and see all the synonyms associated with [an ingredient]," he explained.

What also became clear, Eberhart added, is that the registry provides an opportunity to help the industry manage information more efficiently. "[UL has] experience in multiple industries doing business process automation, what we call robotics," he said. "For example, in the chemical industry, if they change something in a database, it can be automatically updated in all the safety data sheets associated with that product. That is an opportunity in this registry."

## Defining Success

The NIH's ODS Dietary Supplement Database currently contains labels from approximately 50,000 products in the US marketplace.[4] MacKay, however, cautioned that comparing the two databases is tricky because the ODS database may include individual listings for products based on pill count and flavor, which would create duplicate listings, and may not account for discontinued products in its current total.

"[One] of the unique things about this database is that we will be able to tell how many SKUs [stock keeping units] are out there, and which ones are part of a single product," said Eberhart. "Ultimately, we will be able to provide better numbers to the industry."

As such, success is based on full participation, MacKay added. After conversations with critics, media, and regulators, he is confident that the registry is a step in the right direction for manufacturing transparency. "It symbolizes a maturing industry and a willingness to be more transparent, although many critics would like to see a more mandatory program," he said. "But we are satisfied that we can do this on a voluntary basis." HG

**—Karen Raterman**

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## ABC Endorses Supplement OWL

On March 31, 2017, ABC sent a letter to CRN endorsing the new Supplement Online Wellness Library, a self-regulatory initiative spearheaded by CRN for use by the dietary supplement industry to help create a more complete picture of the dietary supplement marketplace in the United States. In the ABC endorsement letter to CRN President Steve Mister, ABC Founder and Executive Director Mark Blumenthal wrote:

> ABC has long advocated for measures by nonprofit organizations and/or members of the botanical and natural products industries to increase sustainability, quality control, transparency, appropriate scientific and clinical research, and responsible communication about the activities and benefits of these ingredients as they are employed in consumer products.
>
> [W]e believe that this new program, in principle, helps fill a vital need in the dietary supplement industry and extended community and the general public — for researchers, health professionals, regulators, members of industry, and consumers to gain relatively easy access to relevant information on specific commercial dietary supplement products in the US marketplace.

ABC encourages its members in the botanical and dietary supplement industry that market branded botanical dietary supplement products to participate in the Supplement OWL by submitting product information for inclusion. More information about the Supplement OWL and how to participate is available from CRN by contacting Gisele Atkinson at gatkinson@crnusa.org, from UL by contacting Erik Eberhart at erik.eberhart@ul.com, or by visiting www.SupplementOwl.org.

# AHP Announces Publication of Monograph and Therapeutic Compendium for Red Clover and Its Extracts

**In March, the American Herbal Pharmacopoeia (AHP) published a new monograph and therapeutic compendium for red clover (*Trifolium pratense*, Fabaceae) flowering tops, aerial parts, and dry extracts.[1] The long-awaited monograph includes a full suite of identity and quality tests, documents historical uses of the plant, and provides a guidance on harvest and cultivation practices, as well as a full review of clinical and pre-clinical pharmacology and safety data.[1]**

AHP monographs are designed to provide a standard for herb purity and identity, help practitioners make educated choices when prescribing botanicals, and serve as a dossier for companies to ensure safety and substantiate dosage and claims, according to AHP Executive Director Roy Upton.

"The AHP monographs are the only such work in the world that we know of that combine a critical review of the traditional knowledge base coupled with the experience of modern clinicians with a critical review of the scientific literature," Upton wrote (email, March 24, 2017). "This provides the most comprehensive and critical review of the therapeutic and safety data on the monographed herb anywhere in the world."

The red clover monograph was initiated and supported by Linnea SA (Riazzino, Switzerland), which makes Promensil, a preparation that contains red clover isoflavones and has been the subject of numerous clinical trials.[2]



**Red Clover** *Trifolium pratense*
Photo ©2017 Steven Foster

Red clover was considered by Seventh-Day Adventist Church founder Ellen White to be "one of God's greatest gifts to man." It has been used historically as an alterative (blood purifier), for infections, boils, skin conditions, vaginal discharge, fever, and inflammation, and to clear the eyes, among many other uses, Upton said. The current primary interest in red clover, he added, is for its use in reducing the severity of symptoms associated with menopause. "Relief of menopause is one of the most sought-after categories in the natural products industry," he said. "This is especially important considering the higher risks of developing reproductive cancers that exist with conventional hormone replacement therapy."

A number of studies, however, have called the efficacy of red clover, and isoflavones in general, into question. As a result, one of the important contributions of the monograph and therapeutic compendium, Upton explained, is to provide accurate, fact-based information and to mitigate biased reporting associated with, for example, concerns over the exposure of phytoestrogens in those with estrogen-sensitive cancers.

"Because phytoestrogens act similarly to estrogens, it stands to reason these should be avoided in those with cancer, especially estrogen-sensitive cancers," Upton wrote. "However, a plethora of scientific data demonstrates no increased risk of cancer when taking isoflavone-containing botanicals like red clover and that there are a number of mechanisms associated with isoflavones that protect and reduce the risk of cancer. This information is especially important for addressing the safety of red clover."

It typically takes AHP, which relies on the work of numerous volunteers and collaborators, about three years to complete a monograph. "The comprehensive nature of the monographs and the extensive peer review they are subjected to by collaborators throughout the world make it a very time-consuming process," Upton wrote.

Specifically in the case of the red clover monograph, AHP used 14 different collaborators and an additional 20 reviewers. Contributors included professional historians, international regulators, agricultural researchers in Canada and the United States Pharmacopeia (USP), and reviewers included herbalists and naturopathic physicians in the United States and Australia, ethnobotanists from Canada and Australia, an obstetrics and gynecology specialist from Austria, and researchers from the University of Illinois-Chicago, among others. The team worked to explain why some studies show efficacy and others do not, and to present the data in a clinically relevant context, which requires in-depth familiarity with the literature and the pharmacological and physiological principles involved. Upton added, "the analytical methodology provided courtesy of USP was under revision, and we thought it best to harmonize with USP than to offer an alternative method." It is typical for AHP to harmonize with European Pharma (EP) or the USP on analytical methods, with a preference for EP because its standard is more reasonable and encompassing, Upton noted (email, April, 12, 2017). In this case, the harmonization did cause a delay in the monograph because USP methods were under revision, and AHP had to re-verify that the methods worked as recorded.

The monograph and therapeutic compendium for red clover is available through AHP's website at www.herbal-ahp.org. PDFs are available for $39.95, and printed four-color versions can be purchased for $44.95. HG

**—Karen Raterman**

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RESEARCH REVIEWS

# Aromatherapy with Damask Rose Essence Reduces Pain Caused by Treatment of Burn Injuries

**Reviewed: Bikmoradi A, Harorani M, Roshanaei G, Moradkhani S, Falahinia GH. The effect of inhalation aromatherapy with damask rose (*Rosa damascena*) essence on the pain intensity after dressing in patients with burns: a clinical randomized trial. *Iran J Nurs Midwifery Res*. May-June 2016;21(3):247-254.**

The severe pain of serious burns is exacerbated by the need to clean, debride, and re-dress wounds daily. Pain control is important in the healing and recovery process. Narcotic and non-narcotic drugs are commonly used for this purpose, but adverse effects and/or increased tolerance may limit their efficacy. The clinical use of inhaled essential oils, generally referred to as aromatherapy, is increasingly becoming accepted as an adjunct pain-control method. and it is used to reduce stress, anxiety, fatigue, and depression, symptoms that often affect patients with burn wounds. Aromatherapy's mechanisms of action, particularly when essential oils are used as inhalants, remain mostly unknown. Damask rose (*Rosa damascena*, Rosaceae) essential oil (DREO) has been little-studied in relation to pain, although some studies report palliative, sleep-promoting, anticonvulsant, and relaxing effects.

This randomized, placebo-controlled, clinical trial investigated the effects of DREO in patients in the burn ward of Besat Therapeutic and Educational Center of Hamadan University of Medical Sciences in Hamadan, Iran. It was conducted from May to October 2013. Patients were 18-65 years of age; could speak, see, and communicate; and had second- and/or third-degree burns. Patients (N = 54) with inhalation, self-inflicted, or electrical burns; burns on the face or eyes; a history of allergies or respiratory illness; or apparent allergy to DREO during the study were excluded. All patients received analgesic and sedative drugs one hour before and immediately after wound dressing.

Data were collected via a questionnaire covering demographic information and the cause and extent of burn wounds. A visual analog scale was used to measure pain intensity (0 = no pain, 1-3 = some pain, 4-6 = moderate pain, and 7-10 = severe pain). For two consecutive days, pain scores were recorded 30 minutes before entering the wound-dressing room and at 15 and 30 minutes after leaving the wound-dressing room. Ten minutes after the initial pain measurement each day, patients in the active group inhaled five drops of 40% DREO (manufacturer information not provided) in distilled water for 20 minutes via gauze pads attached to their collars; those in the control group inhaled five drops of distilled water by the same method. Patients were sent directly to the wound-dressing room after their 20-minute aromatherapy session each day. This intervention was administered by nurses, with patients in the DREO group treated in a different room to avoid carryover between patient groups, without researchers' knowledge. Gauze pads were then removed before patients were treated by researchers whose noses were covered.

Most patients were male (60% in the active group, 52% in the control group), and the average age of patients was 33.2 ± 10.6 years in the active group and 34 ± 12.4 years in the control group. The most common cause of burns was fire (84% in the active group and 96% in the control group); although figures for other causes are not given, caustic substances were mentioned as having caused some. Mean length of hospitalization was 22.5 ± 10.6 days for those in the active group and 22.6 ± 9.7 days for the control group. Patients in the active group had burns over 23.7% ± 8.6% of their bodies, and patients in the control group had burns covering 23.2% ± 8.9% of their bodies. There were no significant differences in demographic characteristics between groups. Four enrolled patients were removed from the study due to discharge from the hospital (one in each group), unwillingness to participate (one in the placebo group), and intolerance of the treatment (one in the active group).

Before the first intervention on day one, the mean pain score was 5.4 in both groups; 80% of patients in the active group and 96% of those in the control group reported moderate pain. At 15 minutes after patients' burns were dressed, average pain scores were 6.8 in the active group and 7.6 in the control group; 68% of patients in the active group and 96% of patients in the control group reported severe pain. At 30 minutes after treatment, average pain scores had diminished to 6.4 in the active group and 7.3 in the control group, with 40% and 92%, respectively, still reporting severe pain. Before the second intervention, mean pain scores were 5.4 in both groups, with 96% of the active group and 100% of the control group reporting moderate pain. At 15 minutes after the second burn dressing, mean pain scores were 6.8 in the active group and 7.6 in the control group, with 72% and 96%, respectively, reporting severe pain. Thirty minutes after the second treatment, mean pain scores were 6.5 in the active group and 7.4 in the control group, with 52% of the active group and 96% of the control group still reporting severe pain.

On both days, there was a statistically significant difference in mean pain intensity between the two groups at 15 minutes ($P$ = 0.010 for day one; $P$ = 0.001 for day two) and 30 minutes ($P$ = 0.001 for both days) after treatment. The increase in pain caused by dressing of burns was significantly less in the active group ($P$ = 0.01). Analysis of variance using repeated measures showed a significant difference in pain severity between the two groups before and after treatment ($P$ = 0.027). Mean pain intensity during the three time periods reported (30 minutes before treatment, 15 minutes after treatment, and 30 minutes after treatment) was significantly different between the two groups ($P$ = 0.001).

This study was small and of short duration, and the effect size was moderate (on average, slightly less than one point on a 10-point scale of pain). Another weakness is that the inactive, unscented placebo would have been obvious to patients so they would not really have been blinded. Future studies should use a control that has an odor but no reported use in pain, and perhaps a third intervention as well that has a reported use for pain management. However, given the intense pain of burn wounds and their treatment, and the low cost and ease of administration of aromatherapy, DREO may be beneficial as an adjunct pain treatment. More research is warranted. HG

**—Mariann Garner-Wizard**




"*Rosa damascena* Aurora." Watercolor by Pierre-Joseph Redouté (1759-1840)
Courtesy of Georges Jansoone

# Aged Garlic Extract Reduces Blood Pressure in Patients with Hypertension

**Reviewed: Ried K, Travica N, Sali A. The effect of aged garlic extract on blood pressure and other cardiovascular risk factors in uncontrolled hypertensives: the AGE at Heart trial. *Integr Blood Press Control*. 2016;9:9-21.**

***Editor's note:*** *This study was supported by a grant from Wakunaga of America Co., Ltd. The company also supplied the study capsules and provided funding for tests and research assistance; however, Wakunaga of America was not involved in the study design, data collection, analysis, or preparation of the manuscript.*

Hypertension, or abnormally high blood pressure, is common around the world and is a risk factor for cardiovascular disease. Multiple clinical trials have reported that aged garlic extract (AGE; *Allium sativum*, Amaryllidaceae) lowers blood pressure. This randomized, double-blind, placebo-controlled trial investigated the effects of AGE on blood pressure, central hemodynamic measures (i.e., those of the central aortic region), and markers of cardiovascular function in adults with hypertension.

The trial was conducted by the National Institute of Integrative Medicine in Melbourne, Australia, between September 2013 and August 2014. Recruitment was directed at adults with "uncontrolled" hypertension, defined as systolic blood pressure (SBP) of at least 140 mmHg and/or diastolic blood pressure (DBP) of at least 90 mmHg. Ultimately, included patients had an SBP of at least 138 mmHg and/or a DBP of at least 85 mmHg. Participants were either not taking medication for hypertension or had been taking it for at least two months before the start of the trial, and their physicians did not plan to change their regimens during the trial. Exclusion criteria included serious health problems (e.g., terminal illness or dementia), secondary hypertension, pregnancy, and use of garlic supplements. Enrolled patients were randomly assigned to either the garlic group or placebo group and took two capsules per day in the evening with food for 12 weeks.

The treatment was Kyolic AGE, which contains 1.2 g of AGE powder standardized to 1.2 mg of *S*-allylcysteine (Reserve formula; Wakunaga of America Co., Ltd.; Mission Viejo, California). The AGE was processed by aging garlic at room temperature for 20 months, which has been shown to affect the concentrations of the potential bioactive compounds. The study article states that placebo capsules were matched to the AGE, but no other description is given. Activated carbon was used in packaging to minimize any difference in odor between the active treatment and placebo, though AGE is already less pungent than fresh garlic. Patients were instructed to keep their medication regimens constant and to keep a daily record of compliance.

Changes in blood pressure were measured at baseline and four, eight, and 12 weeks, and were the primary outcomes. At baseline, physical parameters, exercise, and stress levels were assessed via questionnaires. Central blood pressure (aorta blood pressure), pulse pressure, and other indicators of arterial stiffness (e.g., augmentation pressure) also were measured at baseline and four, eight, and 12 weeks. Fasting blood samples were collected at baseline and at 12 weeks to measure serum cholesterol and triglycerides, inflammation markers, and other parameters. Platelet function also was assessed as a gauge for AGE tolerability, particularly if patients used blood-thinning medications. The overall tolerability of AGE was measured by patient questionnaire.

From 185 patients screened, 104 were randomly assigned, with 55 patients in the AGE group and 49 patients in the placebo group. Following the baseline measurements, three patients in the AGE group and six patients in the placebo group withdrew from the study for personal reasons. At the end of the study, two patients in the AGE group and five patients in the placebo group were excluded due to low compliance (n = 3) or change in blood pressure medication regimen (n = 4, all in the placebo group). The final analysis included 50 patients in the AGE group and 38 patients in the placebo group.

Measurements were not significantly different between groups at baseline. On average, patients were 62.3 ± 11.3 years old and had a body mass index of 27.7 ± 4.9 kg/m$^2$. Patient stress was "comparable" to population levels. In addition, 75% of participants used conventional drugs to treat high blood pressure, and some also used blood-thinning medication, drugs to decrease lipids, and treatments for diabetes and other diseases. At the end of the study, SBP decreased significantly more in the AGE group as compared with the placebo group ($P$ = 0.016). This study included a separate analysis of those who had responded to the AGE treatment, which was defined as a decrease of more than 3% in SBP (at least 5 mmHg) or DBP (at least 3 mmHg). Based on this criteria, 50-60% of patients in the AGE group were considered responders. In this subgroup, there was a substantially greater decrease in SBP (change of 11.5 ± 1.9 mmHg) and DBP (change of 6.3 ± 1.1 mmHg) compared with placebo ($P$ < 0.001 for both). "Non-responders" experienced a small, nonsignificant increase in both SBP and DBP.

Central SBP decreased more in the AGE group than in the placebo group, which approached significance ($P$ = 0.05). Also, there were apparent trends in the AGE group, as compared to the placebo group, toward lowered central pulse pressure ($P$ = 0.08), total vascular resistance ($P$ = 0.06), and mean arterial pressure ($P$ = 0.09) that approached significance. Those in the upper half of pulse wave velocity (PWV) showed a significantly greater velocity decrease in the AGE group as compared with the placebo group ($P$ = 0.02). The change in tumor necrosis factor-α (an inflammation marker) in the AGE group approached significance, as compared with the placebo group ($P$ = 0.05), but this was mostly due to increased values in some patients in the placebo group. No other blood parameters were significantly affected throughout the study.

Compliance in included patients was 96.6 ± 5.6%. Approximately 36% of patients in the AGE group and 26% of patients in the placebo group experienced minor adverse effects such as heartburn, gas, and bloating, mostly during the first week of the study. (A few, mostly in the AGE group, also reported better digestion.) Platelet function, if abnormal, tended to normalize when garlic was taken, while normal function was not affected; there was no interaction with blood-thinning pharmaceuticals.

This study suggests benefits of AGE for hypertension in certain patients, with greater benefit in patients who have more severe pathology. The authors hypothesize that the different patient responses to AGE may be due to individuality; this phenomenon has been reported previously. Certain bioactive compounds in AGE may modulate cellular signaling upstream of vascular function, and bioactivity may be impacted by diet, vitamin status, or genetics. Stated limitations of this study include a greater amount of dropouts in the placebo group, relatively small sample size, and the potential impact of other medications, although it is stated that certain variables were controlled in the statistical analysis. It is also mentioned that additional studies are necessary to clarify effects of AGE on central hemodynamic measures and the causes of inter-individual variability. HG

**—Amy C. Keller, PhD**



**Garlic** *Allium sativum*
Photo ©2017 Steven Foster



# Psilocybin Reduces Symptoms of Anxiety and Depression in Patients with Cancer in Two Clinical Trials

**In December 2016, two clinical trials that investigated the effects of psilocybin on anxiety and depression in patients with cancer were published simultaneously in a special issue of the *Journal of Psychopharmacology*. Psilocybin is a natural psychoactive compound that is found in some species of fungi. One study was conducted by a research team led by Stephen Ross, MD, at the New York University (NYU) School of Medicine,[1] and the other was conducted by a team led by Roland Griffiths, PhD, at the Johns Hopkins University School of Medicine.[2]**

Clinically significant symptoms of anxiety and/or depression are reportedly present in 30-40% of patients with cancer in hospital settings. These symptoms are associated with various negative effects, including medication nonadherence; increased use of health care services; decreased quality of life and social function; increased disability, hopelessness, and pain; desire for hastened death; increased rates of suicide; and decreased survival rates.[1]

A growing body of clinical evidence has linked existential and spiritual wellbeing in patients with cancer with improved quality of life and decreased depression, hopelessness, and suicidality. Therefore, those in the disciplines of palliative care and psycho-oncology have increasingly recognized the need to develop effective therapies in this area, especially since treatment with antidepressant pharmaceutical drugs is associated with delayed symptom improvement, high relapse rates, and significant adverse side effects that compromise treatment adherence.[1]



*Psilocybe azurescens*
Photo ©2017 Paul Stamets

## NYU School of Medicine Study

The purpose of this randomized, double-blind, controlled, crossover study was to investigate the efficacy of a single dose (0.3 mg/kg) of psilocybin (Organix Inc.; Woburn, Massachusetts) compared to a single dose (250 mg) of niacin (vitamin B3, the active control), administered with psychotherapy, to treat clinically significant anxiety or depression in patients with life-threatening cancer. Niacin was chosen to mimic some of the effects of psilocybin (sense of warmth, arousal, tingling sensation, etc.). Patients were randomly assigned to take either psilocybin first (dose one) and then niacin (dose two), or niacin first (dose one) and then psilocybin (dose two). Dose one was administered two to four weeks after baseline assessments, and the crossover occurred seven weeks after dose one, at which time dose two was administered.[1]

Each dosing session lasted eight hours, during which participants were encouraged to lie comfortably and supine while wearing eye shades and listening to standardized music that was "selected by the research team to temporally match the phenomenologic effects of psilocybin over its course of action." Furthermore, each participant was encouraged to focus on their internal experience.[3]

Sixteen participants were randomly assigned to receive psilocybin first. Of those, 14 completed dose one, 12 completed dose two (niacin), and 11 completed the six-month follow-up assessments. Fifteen participants were randomly assigned to receive niacin first. Of those, all 15 completed dose one, 14 completed dose two (psilocybin), and 12 completed the six-month follow-up assessments.[1]

Most of the study participants were recruited from NYU Langone's Perlmutter Cancer Center. Eighteen (62%) of the 29 participants who completed dose one had advanced cancers (stage III or IV). Nine (31%) had breast cancer, eight (28%) had reproductive cancers, five (17%) had digestive cancers, four (14%) had leukemia or lymphoma, and three (10%) had some other type of cancer. Most participants were Caucasian (26, or 90%), female (18, or 62%), and reported having some religious faith (15, or 52%). The average age of participants was 56.3 years, with a range of 22 years to 75 years. The two groups did not differ significantly in terms of demographics or clinical characteristics.[1]

All participants had an anxiety-related diagnosis, with most (26, or 90%) meeting criteria for an adjustment disorder and the rest (three, or 10%) for generalized anxiety disorder (GAD). Before the study, 17 participants (59%) had been treated with conventional antidepressant or anxiolytic medication, but none were taking any psychotropics at the time of study enrollment. In addition, 13 participants (45%) reported no previous history of hallucinogen use.[1]

There were no serious adverse events (AEs) during the trial from psilocybin or niacin. No pharmacological interventions were needed during either dosing session, no psychiatric hospitalizations were required, no participants abused or became addicted to psilocybin, and there were no cases of prolonged psychosis or hallucinogen persisting perception disorder (HPPD). The most common medical AEs attributable to psilocybin were non-clinically significant increases in blood pressure and heart rate (in 22 participants, or 76%), headaches/migraines (in eight participants, or 28%), and nausea (in four participants, or 14%). The most common psychiatric AEs attributable to psilocybin were transient anxiety (in five participants, or 17%) and transient psychotic-like symptoms (in two participants, or 7%; one case of transient paranoid ideation and one case of transient thought disorder). These are all known AEs of psilocybin, and they were transient and tolerable.[1]

Primary outcome variables were anxiety and depression assessed using six measures: the Hospital Anxiety and Depression Scale (HADS) self-rated subscales for anxiety (HADS anxiety) and depression (HADS depression), and the total combined score (HADS total); the Beck Depression Inventory (BDI) self-report depression measure; and the Spielberger State-Trait Anxiety Inventory (STAI) self-report measure of state (STAI state) and trait (STAI trait) anxiety. These measures were assessed at baseline (two to four weeks before dose one), one day before dose one, one day after dose one, two weeks after dose one, six weeks after dose one, seven weeks after dose one (one day before dose two), one day after dose two, six weeks after dose two, and 26 weeks after dose two. The total duration of the study was about nine months.[1]

Participants who received psilocybin first experienced "immediate, substantial, and sustained ... clinical benefits" in all six measures of anxiety and depression symptoms (compared to those who received niacin first) before the crossover that occurred seven weeks after dose one. In addition, those who received psilocybin first experienced significant decreases in all six measures of anxiety and depression compared to baseline immediately after receiving psilocybin. These reductions were significant at each time point, including the final time point at 26 weeks after dose two (niacin), which is equal to about eight months after dose one (psilocybin).[1]

Before the crossover, those who received niacin first experienced either no significant decreases in any of the six outcome measures compared to baseline or transient decreases that became non-significant before dose two (psilocybin). For five of the six primary outcome measures, those who received niacin first experienced significant decreases in anxiety and depression compared to baseline immediately after receiving dose two (psilocybin), and these statistically significant improvements lasted until the end of the study (26 weeks after dose two).[1]

Seven weeks after dose one (one day before dose two), 83% of those who received psilocybin first (compared to 14% of those who received niacin first) met criteria for antidepressant response using the BDI self-report measure, and 58% of those who received psilocybin first (compared to 14% of those who received niacin first) met criteria for anxiolytic response using the HADS anxiety self-rated subscale. At the 26-week post-dose two follow-up (after both groups had received psilocybin), antidepressant or anxiolytic response rates were about 60% to 80%.[1]

There was a significant improvement ($P < 0.05$) in attitudes and adaptations towards death, measured using the Death Transcendence Scale (DTS; a self-report measure of positive attitudes and adaptations towards death), in the group that received psilocybin first (assessed at the 26-week post-dose two follow-up) compared to the group that received niacin first (assessed two weeks after dose one).[1]

At the 26-week post-dose two follow-up, when all participants were asked to reflect on what they thought was their psilocybin session, 52% rated the psilocybin experience as the singular (or in the top five) most spiritually significant experience of their entire lives, and 70% rated it as the singular (or in the top five) most personally meaningful experience of their entire lives. In addition, 87% reported increased life satisfaction or wellbeing because of the experience.[1]

"Single moderate-dose psilocybin, in conjunction with psychotherapy, produced rapid, robust, and sustained clinical benefits in terms of reduction of anxiety and depression in patients with life-threatening cancer," the study authors wrote. "This pharmacological finding is novel in psychiatry in terms of a single dose of a medication leading to immediate anti-depressant and anxiolytic effects with enduring (e.g., weeks to months) clinical benefits. Even though it is not possible to attribute causality of the experimental drug (in terms of sustained clinical benefit) after the crossover, the post-crossover data analyses of the two dosing sequences suggest that the clinical benefits, in terms of reduction of cancer-related anxiety and depression, of single-dose psilocybin (in conjunction with psychotherapy) may be sustained for longer than 7 weeks post-dosing, and that they may endure for as long as 8 months post-psilocybin dosing."[1]

Some limitations of this study were the small sample size, the decreased generalizability that resulted from most of the participants being Caucasian and female, a study design that limited the interpretation of clinical benefits after the crossover, and the use of a control (niacin) with limited blinding.[1]



*Psilocybe semilanceata*
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RESEARCH REVIEWS

**Johns Hopkins University School of Medicine Study**

This randomized, double-blind crossover study compared the effects of a single, very low, placebo-like dose (1 or 3 mg/70 kg [about 0.01 or 0.04 mg/kg]) of psilocybin to the effects of a single high dose (22 or 30 mg/70 kg [about 0.3 or 0.4 mg/kg]) of psilocybin on measures of depressed mood, anxiety, and quality of life, in addition to measures of short-term and enduring changes in attitudes and behavior in patients with cancer. Patients were randomly assigned to take either the low dose first (dose one) and then the high dose (dose two), or the high dose first (dose one) and then the low dose (dose two). Dose one was administered about one month (on average) after baseline assessments, and the crossover occurred about five weeks after dose one, at which time dose two was administered.[2]

The study authors decreased the low dose from 3 mg/70 kg to 1 mg/70 kg after 12 participants because of concerns that 3 mg/70 kg might not adequately serve as an inactive placebo. In addition, they decreased the high dose from 30 mg/70 kg to 22 mg/70 kg because two of the first three participants to receive 30 mg/70 kg were withdrawn from the study (one for vomiting after administration and one for personal reasons).[2]

The low dose of psilocybin was compared to the high dose to minimize the expectancy effects that result when a substance produces highly discriminable effects. Instructions given to participants and study monitors also minimized expectancy effects.[2]

Participants were encouraged to lie down on the couch, use an eye mask, and listen to a music program, which was the same for all participants. In addition, participants were encouraged to focus on their inner experiences.[2]

Twenty-seven participants were randomly assigned to receive the low dose first. Of those, 25 completed dose one, 24 completed dose two (the high dose), and 22 completed the six-month follow-up assessments. Twenty-nine participants were randomly assigned to receive the high dose first. Of those, 26 completed dose one, 25 completed dose two (the low dose), and 24 completed the six-month follow-up assessments.[2]

Participants were recruited through flyers, the internet, and physician referral. Of the 51 participants who completed dose one, 35% had the possibility of cancer relapse, 37% had recurrent/metastatic cancer with more than two years of anticipated survival, and 27% had recurrent/metastatic cancer with less than two years of anticipated survival. Eighteen (35%) had genitourinary cancers, 13 (25%) had breast cancer, eight (16%) had hematologic malignancies, seven (14%) had upper aerodigestive cancer, four (8%) had gastrointestinal cancer, and one (2%) had some other type of cancer. Most participants (94%) were Caucasian, and 49% were female. The average age of participants was 56.3 years. The two groups did not differ significantly in terms of demographics.[2]

Fourteen (27%) of the 51 participants who completed dose one had major depressive disorder (MDD), 11 (22%) had a chronic adjustment disorder with anxiety, 11 (22%) had a chronic adjustment disorder with mixed anxiety and depressed mood, five (10%) had dysthymic disorder, five (10%) had GAD, four (8%) had a dual diagnosis of GAD and MDD, and one (2%) had a dual diagnosis of GAD and dysthymic disorder.[2]

After their cancer diagnoses, 51% of participants had used conventional pharmaceutical antidepressant or anxiolytic medications but had stopped taking these medications before study enrollment. In addition, 45% of participants reported past use of hallucinogens. Participants who reported use of cannabis (*Cannabis* spp., Cannabaceae) or dronabinol (a synthetic cannabis preparation) were asked to not use these at least 24 hours before dosing sessions.[2]

Several AEs occurred during the trial, but none were considered serious. For example, 15% of participants in the high-dose session experienced nausea or vomiting. In addition, 21% of participants in the high-dose session and 8% in the low-dose session experienced an episode of physical discomfort (any type), and 32% of participants in the high-dose session and 12% in the low-dose session experienced psychological discomfort (any type). About a quarter (26%) of participants in the high-dose session and 15% in the low-dose session experienced an episode of anxiety. During the high-dose session, one participant had a transient episode of paranoid ideation. There were no cases of HPPD or prolonged psychosis.[2]

Primary outcome measures were clinician-rated symptoms of depression (measured using the GRID Hamilton Rating Scale for Depression [GRID-HAMD-17]) and anxiety (measured using the Hamilton Anxiety Rating Scale [HAM-A]). These measures were assessed at baseline (about one month before dose one), five weeks after dose one, five weeks after dose two, and about six months after dose two (the six-month follow-up). The total duration of the study was about nine months.[2]

Five weeks after dose one, 92% of those who received the high dose first showed a clinically significant response on the GRID-HAMD-17 (i.e., a decrease of at least 50% compared to baseline), compared to 32% of those who received the low dose first. At the six-month follow-up, 79% of those who received the high dose first continued to show a clinically significant response using this scale. Similarly, five weeks after dose one, 76% of those who received the high dose first showed a clinically significant response on the HAM-A, compared to 24% of those who received the low dose first. At the six-month follow-up, 83% of those who received the high dose first showed a clinically significant response using this scale.[2]

Five weeks after dose one, for those who received the high dose first, the rate of symptom remission (i.e., a decrease of at least 50% compared to baseline and a score of 7 or less on GRID-HAMD-17 or HAM-A) was 60% for depression and 52% for anxiety. At the six-month follow-up for the same group, the rate of symptom remission was 71% for depression and 63% for anxiety. At the six-month follow-up for all participants, the overall rate of clinical response was 78% for depression and 83% for anxiety, and the overall rate of symptom remission was 65% for depression and 57% for anxiety.[2]

Eleven of the 17 outcome measures that were assessed at baseline, five weeks after dose one, five weeks after dose two, and at the six-month follow-up met conservative criteria for demonstrating the efficacy of the high dose of psilocybin. That is, these measures all showed both a significant between-group difference (assessed five weeks after dose one) and a significant difference between the post-dose one and post-dose two assessments in the group that received the low dose first.[2]

The 11 outcome measures that met these criteria were the following: the GRID-HAMD-17, the BDI self-report depression measure, the HADS depression self-rated subscale, the HAM-A, the STAI trait anxiety self-report



*Psilocybe cyanofibrillosa*
Photo ©2017 Paul Stamets

## About Psilocybin

Psilocybin is an indole alkaloid derived from the monoamine alkaloid tryptamine, which, in turn, is derived from the amino acid tryptophan.[4] After ingestion, psilocybin is metabolized to the active compound psilocin, which is also present in psilocybin mushrooms, but in smaller amounts.[5] Psilocin is pharmacologically similar to lysergic acid diethylamide (LSD; a semisynthetic derivative of ergotamine, which is produced by the ergot fungus *Claviceps purpurea* [Clavicipitaceae] and related fungi) and the neurotransmitter serotonin (5-hydroxytryptamine [5-HT]).[4,5] It has been shown that activation of the serotonin receptor subtype 5-$HT_{2A}$ is responsible for most of the psychedelic (i.e., consciousness-expanding and hallucinatory) effects of the compound.[6]

A 1998 review by Guzmán et al. identified 186 fungal species that contain psilocybin and related indoles, or that are likely to contain these substances, with the majority (116, or 62%) of these species belonging to the genus *Psilocybe* (Hymenogastraceae) and the rest belonging to 12 different fungal genera.[7]

Human use of psilocybin mushrooms likely dates back thousands of years. Prehistoric murals from Tassili n'Ajjer in the Sahara Desert in southeastern Algeria, which are thought to be between 7,000 and 9,000 years old, may depict *Psilocybe mairei*. Additionally, a portion of the Selva Pascuala mural, which is located in the municipality of Villar del Humo in Cuenca, Spain, may depict *P. hispanica*. This portion of the mural may be about 6,000 years old, which makes it the oldest known evidence of psilocybin mushroom use in Europe.[8]

In Mesoamerica, the native use of hallucinogenic mushrooms dates back to pre-Columbian times. In his multivolume *Historia General de las Cosas de Nueva España*, Franciscan friar Bernardino de Sahagún (1499-1590) recorded the ritualistic use by the Aztecs of psilocybin mushrooms that they called *teonanácatl* (which translates approximately to "God's flesh" in Náhuatl). De Sahagún reportedly wrote that mushroom intoxication gave the Aztecs the ability to seemingly change themselves into animals and have powerful visions during which they heard voices they believed to be from God.[9]

After participating in a Mazatec ritual in Oaxaca, Mexico, which involved psilocybin mushrooms, the amateur mycologists Robert Gordon Wasson, a vice president of J.P. Morgan and Co., and his wife Valentina published a 1957 article in *Life* magazine titled "Seeking the Magic Mushroom." This article sparked widespread interest in psilocybin mushrooms and reportedly inspired some, including Harvard psychologist Timothy Leary, PhD, to study and popularize psilocybin and other entheogens (i.e., substances that produce an unordinary state of consciousness for religious or spiritual purposes; in Greek, entheogen means "generating the divine within").[9]

In 1959, Swiss chemist Albert Hoffman (who was the first to synthesize LSD in 1938) isolated the active principle psilocybin from *Psilocybe mexicana*. In the 1960s and 1970s, hallucinogens, including psilocybin and LSD, were the subjects of multiple studies, but this research stopped for almost three decades after the US Controlled Substances Act of 1970 placed these substances into Schedule I, the most restrictive and punitive schedule. This was done because of concerns about widespread non-medical use of these compounds.[1,2]

Psilocybin is not known to be addictive and may have anti-addictive properties. It also has a well-established safety profile in human laboratory and clinical trial research. According to Ross et al., since the early 1990s, about 2,000 varying doses of psilocybin have been safely administered to humans in the United States and Europe, in carefully controlled clinical settings.[1]

Psilocybin mushrooms can induce a sense of exhilaration, hallucinations that include vivid and bright colors and shapes, euphoria, distorted perception of time, and impaired judgment. Stationary objects may appear mobile. In addition, although visual hallucinations are more common, auditory hallucinations can also occur. Hallucinations typically do not last longer than four or five hours.[4]

measure, the Profile of Mood States (POMS) total mood disturbance subscale (a self-rated dysphoric mood measure), the Brief Symptom Inventory (BSI; self-rated psychiatric symptoms), the McGill Quality of Life (MQOL) self-rated measure of overall quality of life (total score) and meaningful existence (existential subscale), the Life Attitude Profile-Revised (LAP-R) death acceptance self-rated scale, and the Life Orientation Test-Revised (LOT-R) self-rated optimism measure.[2]

Furthermore, mystical experience scores, measured using the Mystical Experience Questionnaire (MEQ30), assessed immediately after dose one, correlated significantly with 18 of 20 measures that were assessed five weeks after dose one.[2]

"The data show that psilocybin produced large and significant decreases in clinician-rated and self-rated measures of depression, anxiety or mood disturbance, and increases in measures of quality of life, life meaning, death acceptance, and optimism," the study authors wrote. "These effects were sustained at six months."[2]

In addition, participants attributed positive changes in attitudes about life, self, mood, relationships, and spirituality to the high-dose experience, "with over 80% endorsing moderately or higher increased well-being or life satisfaction," the authors continued.[2]

Also according to the authors, "the significant association of mystical-type experience (MEQ30) during [dose one] with most of the enduring changes in therapeutic outcome measures five weeks later is consistent with previous findings showing that such experiences on session days predict long-term positive changes in attitudes, mood, behavior, and spirituality."[2]



*Psilocybe cubensis*
Photo ©2017 Paul Stamets

## Conclusion

There has been a relatively recent resurgence of interest in using psychedelic substances, including psilocybin and LSD, for clinical therapeutic purposes. These two trials, which are reportedly the most rigorous trials to date using psilocybin, are part of that resurgence. According to Griffiths et al., this resumption of research has helped establish conditions for safe administration of psilocybin.[2] In addition, according to Ross et al., the finding that a single dose of psilocybin can lead to significant antidepressant and anxiolytic benefits that can last weeks, if not months, is novel in psychiatry.[1] Despite psilocybin's Schedule I status, these trials suggest that it may have therapeutic potential for addressing existential distress in patients with cancer, and may also indicate that further trials are warranted. HG

**—Connor Yearsley**

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# Assessment of the Medicinal Chemistry of Curcumin: When a Plant-Derived Natural Product Is Not a Suitable Conventional Pharmaceutical Drug Lead

**Reviewed: Nelson KM, Dahlin JL, Bisson J, Graham J, Pauli GF, Walters MA. The essential medicinal chemistry of curcumin [published online January 11, 2017]. *J Med Chem*. doi: 10.1021/acs.jmedchem.6b00975.**

Curcumin is one of the major constituents of turmeric (*Curcuma longa*, Zingiberaceae), which has been used as a food, spice, and traditional medicine for thousands of years. Curcumin isolated from the plant's rhizome has been studied as a therapeutic agent for many different conditions and diseases.

This review evaluated the medicinal chemistry of "curcumin" to determine if it is a suitable lead for the development of conventional pharmaceutical drugs. "Curcumin" is often used ambiguously in the scientific literature to refer to both the individual compound and mixtures of curcuminoids, which represent some of the alleged biologically active compounds in turmeric root and its extracts. Therefore, the authors of the review use "curcumin" interchangeably with "curcuminoids." The authors also attempt to distinguish traditional botanical uses of chemically complex turmeric root/rhizome preparations from the more chemically focused and concentrated curcumin preparations, noting that the observed activity of the turmeric and curcumin-rich preparations cannot be explained solely by the putative activity of curcumin.



**Turmeric** *Curcuma longa*
Photo ©2017 Steven Foster

Although the review focuses on curcumin, the paper may also serve as a general guide on how to assess natural products (or, more specifically, pure compounds derived from chemically complex plant material) as potential candidates for pharmaceutical drug development. According to the authors, ideal conventional drug candidates are chemically stable and have high water solubility, potent and selective target activity, high bioavailability, broad tissue distribution, stable metabolism, and low toxicity. The review presents evidence that curcumin, as a single chemical entity or as a combination of related curcuminoids, does not exhibit these properties, although there does not seem to be any evidence that pure curcumin or collective curcuminoids are toxic at levels normally associated with their presence in orally consumed curcumin-rich dietary supplement preparations.

After analyzing the relevant scientific literature, the authors found high variability in reported "curcumin" purity and/or overall composition, in addition to a "widespread lack of characterization of 'curcumin' materials." Despite most commercial "curcumin" ingredients and finished products containing multiple compounds (e.g., the curcuminoids curcumin, demethoxycurcumin, and bisdemethoxycurcumin), the specific composition was not always defined in the reviewed articles (and/or on the tested products' labels). The authors note that this variability in commercial curcumin preparations is an obstacle to interpreting and reproducing experimental results.

According to the authors, curcumin exhibits all behaviors of pan-assay interference compounds (PAINS),[1-9] which tend to give false positives in assay readouts. Assay interference may result from various properties or "behaviors" of PAINS, including covalent labeling of proteins, metal chelation, redox reactivity, aggregation, membrane disruption, fluorescence interference, or structural decomposition. Curcumin, which has a high number of reported bioactivities,[10] has been shown to do all of the above. Thus, the authors caution that "any report of [curcumin] activity in an assay that does not either exclude or account for these potential modes of assay interference should be treated with caution."

The review also discusses potential concerns regarding the stability of curcumin. The concentration of the compound reportedly decreases by 50% within 20 minutes at neutral pH, room temperature, and in an aqueous buffer solution. While curcumin is more stable in acidic environments (i.e., solutions with a pH of less than seven), curcumin becomes less water-soluble as the pH of its envi-

ronment decreases.[11-13] The authors state that "Nearly all the manuscripts reviewed failed to consider the stability of [curcumin]," and that the "time frame for [assays] described in publications included in NAPRALERT allows for significant degradation of curcumin."

In addition to stressing the importance of the initial characterization of the curcumin material, the authors note that it is imperative to identify amounts of degradation products present at the end of an experiment.[14] "The polypharmacology of curcumin may in part, or even largely, be due to the sum of its degradation products. Instability of curcumin must be considered when interpreting bioassay results, if stability is not otherwise demonstrated. Curcumin stability can be improved with lipid encapsulation or nanoparticles, but these will have to be evaluated as new compounds with potential cytotoxicity."

The authors also point out that "Curcumin also displays undesirable physicochemical properties relative to known drugs." The main concern is that curcumin forms chemical aggregates (colloids) under many common bioassay conditions. Enzymes, which are often targeted in standard bioassays, can be inhibited by colloids.[15,16]

Curcumin bioactivity was often observed at concentrations typically above the critical aggregation concentration threshold for curcumin. In addition, the authors found that "appropriate counterscreens for assay interference were frequently not performed, and target engagement was not confirmed nor was target selectivity." Identifying the locations of cellular targets is important, "as curcumin has been shown to perturb cell membranes," which can be "mistaken for specific binding to membrane-associated proteins."[7]

The authors then discuss curcumin's pharmacokinetic properties, which are described as "generally accepted … as poor."[17,18] This review evaluated whether curcumin has suitable absorption, distribution, metabolism, excretion, and toxicology for a "drug lead." In all clinical studies reviewed, the authors found no detection of curcumin in the serum of the majority of subjects tested. While distribution of curcumin in humans has been "sparingly studied," rodent models suggest that curcumin has a high variability in distribution.[18-20] The authors state that this variability could be due to differences in material, extraction, preparation, detection methods, or lack of specificity in detection assays used.

Extensive research has examined curcumin metabolism in human liver microsomes and has shown a high potential for modification by both first and second phase metabolism. Regarding excretion, rodent studies show that the majority of curcumin is excreted in the feces, while small amounts may be absorbed and excreted unchanged, or not absorbed at all and passed directly to feces. Metabolized curcumin is excreted in urine as glucuronide and sulfate conjugates.

Regarding its toxicology, curcumin has been shown to interact with human enzymes (e.g., cytochrome P450s and glutathione S-transferase) that have been implicated in the occurrence of adverse events or interactions with conventional pharmaceutical drugs. Curcumin has been reported as toxic to many cancer cells lines, but it has been reported as toxic to normal human cells in only a few studies.[21,22] The authors caution those who seek to improve the pharmacokinetics of curcumin, as they could increase these potential cytotoxic effects.[21] They hypothesize that curcumin's high observed tolerance in humans and low rate of reported adverse events is "likely due to [its] … poor absorption and low bioavailability." However, the authors also mention that curcumin's reported human health benefits could potentially be due to its effects on the gut microbiome,[17] which would make absorption moot. As they explain, "it may be possible for curcumin to have an effect on human health without being absorbed. Emerging research suggests that it could affect the gut microbiota, which has been linked to several chronic diseases."

One common theme the authors found disturbing is that "published bioactivity data of curcumin are typically not evaluated critically before [they are] used to justify further research." Therefore, they urge researchers to assess the medicinal chemistry of bioactivity assays before moving forward with further research.

The authors remain skeptical that oral curcumin supplementation (as a single compound) has any effect on human health, and their review of clinical trials does not support further investigation into curcumin as a conventional pharmaceutical therapeutic agent.

Overall, the review concludes that curcumin does not possess the properties required for a reliable conventional drug candidate. However, while isolated curcumin may not be a viable conventional therapeutic according to this review, the authors acknowledge that natural products require a holistic approach. As they explain: "there is increasing evidence that [chemically complex traditional medicine] agents cannot be described with reductionist pharmacology models."[23]

This article was covered fairly extensively in the mainstream media in the United States with the misleading message that turmeric and/or turmeric extracts standardized to curcumin have been found to be ineffective. Major national publications featured headlines such as "Turmeric May Not Be a Miracle Spice After All" (*TIME*, January 12, 2017), "Everybody Needs To Stop With This Turmeric Molecule" (*Forbes*, January 18, 2017), and "Turmeric May Be Tasty, But It's Not a Cure-All" (*Smithsonian Magazine*, January 13, 2017).[24-26]

**—Alexis Collins, MA, MS**

## ABC Comments

The different uses of "curcumin" as a conventional drug and as a primary ingredient in curcumin-rich dietary supplements must be distinguished. In addition, caution must be taken when interpreting in vitro data based on this pure compound, a group of curcuminoids, or their mixtures with other constituents, and extrapolating the observed effects into activities in humans. Curcumin has produced positive results in many of these in vitro tests, and some of these results are likely due to assay interferences, as detailed by the authors, rather than actual bioactivity. Based on the available data, the usefulness of curcumin as a conventional drug (e.g., to treat cancer or Alzheimer's disease) is limited.

However, this does not mean that turmeric and products made from turmeric do not have beneficial bioactivities — a point also highlighted by the authors. The use of certain "curcumin" ingredients (e.g., turmeric extracts or powdered turmeric rhizome) as a dietary supplement, in particular to address inflammatory conditions, has merit and warrants further investigation. The limitations in bioavailability and stability of curcumin are well-known and can be addressed to some extent by improving the formulations, as has been done with some commercial turmeric extracts. Clinical studies that reported positive results with "curcumin" in the area of osteoarthritis, for example, have been published. Therefore, the authors' statement that "curcumin … has never been shown to be conclusively effective in a randomized, placebo-controlled clinical trial for any indication" may be based on very strict requirements for substantiating conclusive efficacy.

In addition, the use of turmeric preparations on a regular basis may have some disease-preventing effects. Demonstrating a preventive effect scientifically is particularly challenging, since extensive long-term investigations on relatively large test populations are needed. However, the available data, although incomplete, may suggest that turmeric can be beneficial for the prevention of certain inflammatory diseases, and possibly other diseases as well.

Finally, the authors raise an interesting point about curcumin's health benefits potentially stemming from its interactions with the gut metabolome. They note: "As an alternative approach, it may be possible for curcumin to have an effect on human health without being absorbed. Emerging research suggests that it could affect the gut microbiota, which has been linked to several chronic diseases." HG

**—Stefan Gafner, PhD**

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# A Snapshot of the Modernization of Traditional Chinese Medicines in Hong Kong

## A Fulbright Scholar's Perspective

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In the shadows of some of Hong Kong's modern skyscrapers are TCM pharmacies that have changed little since colonial days. Photo ©2017 Wesley Chan



Traditional wooden drawers filled with bulk botanical TCM ingredients can be found in many TCM pharmacies like this one at the Integrative Medical Centre, Faculty of Medicine, The Chinese University of Hong Kong. Photo ©2017 Wesley Chan

***Editor's note:*** *As part of an eight-month Fulbright Scholar Program-sponsored sabbatical in 2014-2015 at the Institute of Chinese Medicine at the Chinese University of Hong Kong, one of the authors of this article (EJK), a pharmacognosist and natural product chemist, conducted research and interviews in collaboration with a local expert (CBSL) on traditional Chinese medicine (TCM) and pharmacy to learn more about the modernization of TCM in Hong Kong. His field research included visits to local herbal markets, TCM clinics, hospitals with Chinese medicine dispensaries, and local Chinese herbal pharmaceutical companies. As detailed in this article, the authors observed a range of approaches to TCM: Some practitioners are employing techniques that have been used for thousands of years, and others are embracing changes that have come about from new technologies.*

**The announcement of the Nobel Prize in Physiology or Medicine in October 2015 brought traditional Chinese medicine (TCM) to the front-and-center of the minds of people around the world. After extensively reviewing TCM formulae as part of a public health initiative in the People's Republic of China almost 50 years ago, one of the awardees, Tu Youyou, was recognized for her research team's discovery of a new treatment for malaria: artemisinin, a compound found in the Chinese medicinal herb *qinghao* (*Artemisia annua*, Asteraceae).[1,2] After millennia of practice, TCM continues to be used and studied around the world, and it has evolved in modern times.**

*Panax notoginseng*
Photo ©2017 Steven Foster



The traditional practice of Chinese medicine involves diagnoses by trained Chinese medicine practitioners and prescriptions of TCM formulae, which can be administered in various ways. (TCM encompasses many modalities from acupuncture to medicines composed of plant, animal, and mineral products, but this article will focus on botanicals used in TCM.) Typically, these formulae include various raw herbal materials that must be boiled in water prior to ingestion (decoctions), or dried herbal materials or desiccated boiled-water extracts that can be taken in pill form. Often, a formula would be consumed once or twice daily. Before the establishment of Hong Kong's Chinese Medicine Ordinance (Chapter 549 of the Laws of Hong Kong) in 1999,[3] practitioners of Chinese medicine were not legally required to be registered in order to dispense medicines. Today, there are more than 7,000 registered Chinese medicine practitioners in Hong Kong.

Hong Kong is ranked highly in a number of international indices for its public health system and economy, and is one of Asia's wealthiest and most modern cities.[4,5] Although there are many Western medical doctors and clinics in Hong Kong, a strong belief in the use of TCM remains. Many of the findings presented here reflect changes that are occurring with TCM practice in the People's Republic of China, as well as worldwide.

Hong Kong is on the cutting edge of many of these changes due to its strong economic position in the world and modern research facilities, such as those at the Chinese University of Hong Kong, Institute of Chinese Medicine (CUHK-ICM). A new era in TCM practice in Hong Kong can be traced back to 1997 when Hong Kong was returned by Great Britain to the People's Republic of China, and the Chief Executive of the Hong Kong Special Administrative Region announced the government's intention to set up a formal regulatory framework for TCM.[6] In the decades that followed, Hong Kong has developed a thriving and regulated TCM marketplace.

### Thriving Tradition with a Modern Backdrop

In the narrow streets of Ko Shing Street Herbal Market in Hong Kong's Sheung Wan neighborhood, there are numerous stores, clinics, and even small manufacturers of TCM products that, at first glance, have changed little since Hong Kong's colonial period. Stores have bulk herbs displayed in barrels and glass containers. Some high-end TCM pharmacies have the traditional wooden drawers devoted to different herbs, and workers still use old-fashioned balance scales to weigh them. It is a stark contrast to Hong Kong's modern skyline, with skyscrapers like the 417-meter (1,368-foot) International Finance Centre Two less than two kilometers (1.2 miles) away. The quality of raw herbs from these suppliers and pharmacies can vary significantly, as we found, for example, in our studies on astragalus (*Astragalus membranaceus*, Fabaceae) root.[7]

There are more than 500 Chinese herbal medicines listed in Schedule 2 of the Chinese Medicine Ordinance,[8]

and about 200 of them are commonly used in the local community in Hong Kong.[6] A list of 10 common TCM botanicals in Hong Kong — mostly based on the first volume of *Hong Kong Chinese Materia Medica Standards*[6] — is provided in Table 1.

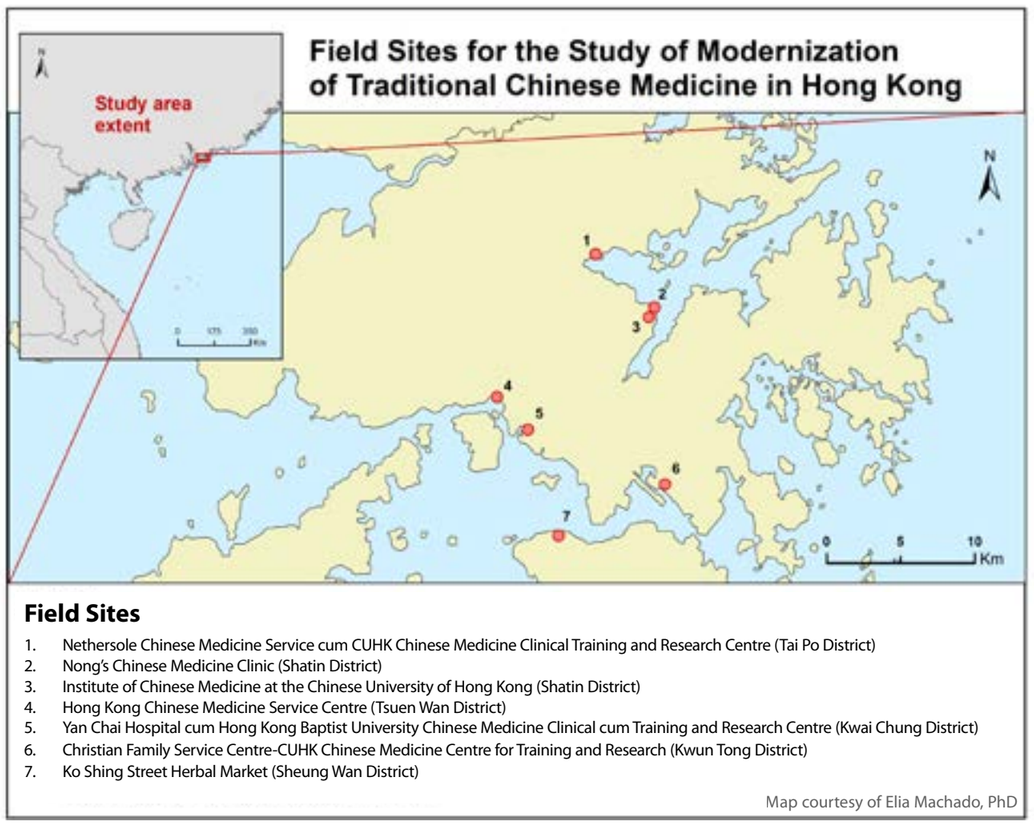
In the TCM clinics of Ko Shing Street and other parts of Hong Kong, one will encounter many highly experienced TCM practitioners working out of herbal stores. This contrasts with the modern environment of certain clinics like the Hong Kong-based chain store Nong's Modernized Chinese Medicine Clinic, which has 52 modern, modular clinics mostly in shopping malls throughout Hong Kong. At these clinics, TCM practitioners in white coats formulate and dispense processed TCM prescriptions using high-end electronic instruments and innovative technology. While the ancient forms of TCM are still widely practiced in Hong Kong, we observed a growing trend in modernization in the clinics and beyond.

## Modern Approaches to Distributing TCM

It is not easy to sustain the often time-consuming practice of TCM treatments in Hong Kong where Western alternatives are readily available and the pace of life does not lend itself to long preparation times. For example, when preparing a Chinese herbal decoction, patients are traditionally instructed to boil complex mixtures of processed raw herbs in water for a period of one to two hours. Such practice is no longer feasible for many residents of Hong Kong with long working hours.

Based on our visits to seven different TCM clinics and local Chinese herbal pharmaceutical companies in Hong Kong (see map below), we observed a trend toward simplifying TCM in several specific ways. First, there has been an effort to create TCM formulae that contain fewer herbs, and that can be marketed as proprietary Chinese medicines or health supplements at local pharmacies for the general public. Patients can simply go to a pharmacy to purchase these products, which do not require a prescription from a TCM practitioner. However, one drawback to using these ready-made formulations is that they do not take into account the personalized medicine approach, which is still regarded as an important part of TCM philosophy.

In addition, many TCM practitioners at both private and public clinics in Hong Kong prescribe extracts that have been processed into granules, which can be dissolved readily in water. Granules are produced by boiling TCM ingredients in water, concentrating the resulting extract (often in a 5:1 ratio), and then spray-drying the extract onto an excipient, such as dextrin. Granules are becoming more popular because they can be easily prepared by TCM practitioners




### Field Sites

1. Nethersole Chinese Medicine Service cum CUHK Chinese Medicine Clinical Training and Research Centre (Tai Po District)
2. Nong's Chinese Medicine Clinic (Shatin District)
3. Institute of Chinese Medicine at the Chinese University of Hong Kong (Shatin District)
4. Hong Kong Chinese Medicine Service Centre (Tsuen Wan District)
5. Yan Chai Hospital cum Hong Kong Baptist University Chinese Medicine Clinical cum Training and Research Centre (Kwai Chung District)
6. Christian Family Service Centre-CUHK Chinese Medicine Centre for Training and Research (Kwun Tong District)
7. Ko Shing Street Herbal Market (Sheung Wan District)

Map courtesy of Elia Machado, PhD






*Salvia miltiorrhiza*
Photo ©2017 Steven Foster



*Angelica sinensis*
Photo ©2017 Steven Foster


*Astragalus membranaceus*
Photo ©2017 Steven Foster

### Table 1. Ten Botanicals Commonly Used in Hong Kong TCM Practice

| Common Name (Pinyin) | Chinese Name | Latin Binomial | Chinese Materia Medica/ Pharmacopeial Name |
|---|---|---|---|
| *Zexie* | 澤瀉 | *Alisma orientale* (Alismataceae) | Alismatis Rhizoma |
| *Danggui* | 當歸 | *Angelica sinensis* (Apiaceae) | Angelicae Sinensis Radix |
| *Huangqi* | 黃芪 | *Astragalus membranaceus* (Fabaceae) | Astragali Radix |
| *Gancao** | 甘草 | *Glycyrrhiza glabra, G. inflata, G. uralensis* (Fabaceae) | Glycyrrhizae Radix et Rhizoma |
| *Danpi* | 牡丹皮 | *Paeonia suffruticosa* (Paeoniaceae) | Moutan Cortex |
| *Renshen* | 人參 | *Panax ginseng* (Araliaceae) | Ginseng Radix |
| *Sanqi* | 三七 | *Panax notoginseng* (Araliaceae) | Notoginseng Radix |
| *Guanhuangbo* | 關黃柏 | *Phellodendron amurense* (Rutaceae) | Phellodendri Amurensis Cortex |
| *Huangbo* | 川黃柏 | *Phellodendron chinense* (Rutaceae) | Phellodendri Chinensis Cortex |
| *Danshen* | 丹參 | *Salvia miltiorrhiza* (Lamiaceae) | Salviae Miltiorrhizae Radix et Rhizoma |

* In TCM, a single common name may refer to more than one botanical species.


*Paeonia suffruticosa*
Photo ©2017 Steven Foster


*Glycyrrhiza uralensis*
Photo ©2017 Steven Foster

at local pharmacies using modern dispensary equipment. They are also more convenient for patients to consume because they need only to dissolve the granules in a cup of hot water. In fact, the TCM pharmacies operated by the Hong Kong Hospital Authority are dispensing processed raw herbs or granules obtained from a contracted supplier, per patient preference. According to the Hong Kong Hospital Authority, its TCM clinics dispensed about half of its prescriptions as granules in 2014.[9] Some studies have found that although granules aim to standardize dosages of a particular botanical, the method by which the granule is produced can lead to variable dosages.[10] Although granules are becoming more popular in Hong Kong and throughout Asia, many patients still prefer to have the TCM prepared from the original materials as a water extract or strong tea or tisane (i.e., a decoction). Because of this, some pharmacies provide TCMs as prepared extracts that are given to patients in liquid form that can be consumed directly, and can provide up to a two-week supply. Some even provide same-day courier delivery service to patients within certain areas of Hong Kong.

## Quality Control Measures

The safety of TCM is critical for its public acceptance, especially in light of well-publicized problems with some Chinese botanicals. (For example, in the early 1990s, a weight-loss supplement that contained the nephrotoxic and potentially carcinogenic herb *Aristolochia fangchi* [Aristolochiaceae] caused more than 100 women in Belgium and France to sustain kidney damage.[11]) The testing and certification industry in Hong Kong is based on internationally recognized standards and is considered to have a high level of integrity and credibility. From the limited observations of one of the authors (EJK), Hong Kong people seem to be acutely aware of problems with product adulteration in the neighboring People's Republic of China, since they witness, on a daily basis, people traveling from the mainland to Hong Kong to purchase items that have a history of being adulterated in China.[12] At Hong Kong pharmacies, it is a common experience to see mainland people with large rolling suitcases filled with such products to bring back home.

Hong Kong has established its own standards for TCM (the *Hong Kong Chinese Materia Medica Standards*[6]) that include authentication and quality analyses. There are also safety tests for heavy metals, pesticides, and microbial limits that are conducted by laboratories accredited by the Hong Kong Laboratory Accreditation Scheme. The Hong Kong Hospital Authority has established even stricter requirements for TCM ingredients distributed by its clinics, such as tests for dyes (e.g., auramine O), foreign matter, and toxic substances (e.g., aconitine, atropine, and aristolochic acid — potentially toxic constituents of plants in the genera *Aconitum* [Ranunculaceae], *Atropa* [Solanaceae], and *Aristolochia*, respectively).

In summary, there seems to be a strong commitment to the modernization of TCM in Hong Kong, and great efforts have been made to simplify the practice for the ease of modern peoples' lives, and to ensure their safety.

## Recent Development of Education and Research in TCM

TCM clinical practices and pharmacies in Hong Kong are mostly private. However, the Hong Kong Hospital Authority has partnered with non-governmental organizations and three universities in Hong Kong to support 18 TCM clinics, which had more than one million combined visits in 2014.[8] Three Hong Kong universities offer bachelor's of science programs in Chinese medicine: Hong Kong Baptist University, CUHK, and The University of Hong Kong. In recent years, some universities have started to offer bachelor's of pharmacy programs in Chinese medicine and various master's of science programs in Chinese medicine, acupuncture, and other specialized areas. Some Hong Kong universities also have established bachelor's of science programs in testing and certification that include TCM in their curricula.

The CUHK-ICM has a mission to modernize Chinese medicines through scientific research. The institute has made great attempts to provide scientific evidence that supports the use of Chinese medicines as alternative or complementary therapies in diseases that are not well-managed by Western conventional medicines; to develop evidence-based Chinese medicines for the prevention and treatment of chronic diseases; and to transform the promising research output into commercial, evidence-based herbal health supplements. The authentication team ensures good quality control of the medicinal herbs for both laboratory (animal- and cell-based assays) and human clinical studies. Different research laboratory platforms have been established for the mechanistic studies of different disease areas as well. In addition, through collaboration with various clinical departments at the Prince of Wales Hospital, the efficacy of various herbs and herbal formulae have been further verified in clinical trials.[13]

## Overall Impressions

In her Nobel Laureate address in Stockholm, Sweden, on December 7, 2015, Tu Youyou noted that there was potential for great new medical discoveries by integrating the best practices of Western medicine and TCM.[2] Modern TCM in Hong Kong is certainly moving along that road, from the standardization of medicines to clinical and mechanistic studies. It is an exciting time for TCM development in Hong Kong and beyond, and there have been substantial efforts by CUHK-ICM and other research institutions to use cutting-edge scientific tools to assess the safety and efficacy of many traditional Chinese medicines. With this investment in TCM, the future holds significant opportunities for its increased acceptance by people throughout the world. HG


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A TCM pharmacy technician in a Hong Kong Hospital Authority clinic uses a traditional balance scale (sometimes called an "opium scale" by non-Chinese) to weigh botanical TCM ingredients for a prescription. Photo ©2017 Edward J. Kennelly



Above: A shift from raw to processed botanicals in the form of granules is becoming popular in many TCM pharmacies, like this one at the Integrative Medical Centre, Faculty of Medicine, The Chinese University of Hong Kong. Photo ©2017 Wesley Chan

*Citrus reticulata*
Photo ©2017 Wesley Chan



# THE VENUS FLYTRAP

## Conserving the Carnivorous Curiosity

**By Connor Yearsley**

In his book *Insectivorous Plants*, which was first published in 1875, English naturalist and evolutionary biologist Charles Darwin wrote that the Venus flytrap (*Dionaea muscipula*, Droseraceae) "is one of the most wonderful [plants] in the world."[1]

Now, that "wonderful" plant is being threatened in the wild by a combination of poaching, overharvesting, habitat loss, fire suppression, wetland drainage, seed collection, and other factors.[2-4]

Based on information from the North Carolina Natural Heritage Program's database, it is estimated that approximately 73,000 to 158,000 individual plants remain in the wild. "This may sound like a lot, but these populations are very imperiled and the threats to these populations are high," wrote Laura Robinson, a botanist with the Natural Heritage Program (email, April 4, 2017).

The Venus flytrap is native to a small area in southeastern North Carolina and northeastern South Carolina,[5] but it has reportedly been naturalized in other states, including Florida and New Jersey.[6] Specifically, it is found within an approximately 75-mile radius of the port city of Wilmington, North Carolina.[2] The colonial governor of North Carolina, Arthur Dobbs, who may have been the first to document the species, noted the plant's limited geographical range in a 1759 letter to his friend, English botanist Peter Collinson: "We have a kind of Catch Fly Sensitive which closes upon anything that touches it. It grows in this latitude 34 but not in 35°."[7]

According to the book *Dionaea: Venus's Flytrap* (Redfern Natural History Productions, 2012), the Venus flytrap has been entirely eliminated from about 1.5 million acres of habitat across the northeastern part of its natural range, and has also been eliminated from south and central parts of its range. Although a few populations persist along the extreme western periphery of the plant's range in the Sandhills region of North Carolina,



"Venus's Fly-trap." Illustration from *Directions for Bringing Over Seeds and Plants, from the East-Indies and Other Distant Countries* by John Ellis (1710-1776). Image courtesy of Linda Hall Library Digital Collections.





**Venus flytrap** *Dionaea muscipula*
Photo ©2017 Cathy Keifer

People find [flytraps] in their backyards occasionally. And we know of a couple of spots where they are likely, but the property is in private hands. It is fair to say that most of the flytraps are on property owned by The Nature Conservancy, other land trusts, the government [state and federal], and the US Department of Defense.

When poachers are caught it is often because authorities have been tipped off by other poachers who are protecting "their turf," or by others, such as bird watchers or hikers.



**Venus flytrap**
*Dionaea muscipula*
Photo ©2017 Steven Foster

these populations are separated by more than 50 miles from all other Venus flytrap sites. Furthermore, most of the limited remaining populations include less than 500 individual plants, and the authors consider it unlikely that these populations will be viable in the long term.[4]

In addition to capturing insects, arachnids, and occasionally even small frogs and snails,[8] the Venus flytrap, like other carnivorous plants, has captured the imagination of many people for years. Exaggerated depictions of carnivorous plants, often oversized and man-eating, have been featured prominently in fictional works, such as Sir Arthur Conan Doyle's 1880 short story *The American's Tale: An Arizona Tragedy*, John Wyndham's 1951 novel *The Day of the Triffids*, and the 1960 film and subsequent musical *The Little Shop of Horrors*[9] (and the 1986 film adaptation of the musical). Fascination (propelled by Darwin's 1875 book), and perhaps often obsession, with carnivorous plants in general and with the Venus flytrap in particular have led to extensive harvesting of the plant in the wild, and this is one of the main causes of its decline.



Courtesy of The Nature Conservancy

## Current Outlook

### *Poaching*

The Venus flytrap became officially protected by North Carolina legislation in 1956, but overharvesting has remained a problem for decades.[2] In 1981, it was estimated that between 1.4 million and 4.5 million plants were sold annually within the United States, the majority of which were thought to be of wild origin. In 1990, 1,077,227 plants (mostly bulbs, but 200,000-300,000 whole plants) were exported from North Carolina, and no plants were exported from South Carolina.[10]

On December 1, 2014, it became a felony in North Carolina for any person to dig up, pull up, take, or aid in taking or carrying away a Venus flytrap plant, or the seed thereof, growing on the land of another person, or from the public domain, without a permit signed by the landowner. Previously, this was a misdemeanor, punishable by a maximum fine of $50, but offenders can now face up to two years or more in prison.[2,11]

In South Carolina, it is a misdemeanor to "cut, collect, break or otherwise destroy" Venus flytrap plants on private or public property without the owner's consent. If convicted, offenders "shall be fined not more than two hundred dollars or imprisoned not more than thirty days nor less than five days. Each violation shall constitute a separate offense."[12] In the past, Venus flytrap poaching has apparently been "minimal" in South Carolina, where a small percentage of the plants occur.[10]

The Venus flytrap grows in boggy areas with moist, acidic soil that is usually low in nutrients.[6] "People find them in their backyards occasionally," wrote Debbie Crane, director of communications for the North Carolina chapter of The Nature Conservancy (TNC), a nonprofit conservation organization that works around the world to protect ecologically important lands and waters for nature and people (email, March 28, 2017). "And we know of a couple of spots where they are likely, but the property is in private hands. It is fair to say that most of the flytraps are on property owned by TNC, other land trusts, the government [state and federal], and the US Department of Defense."

In January 2015, four men were arrested for poaching Venus flytraps on the Holly Shelter Game Land preserve. Although TNC originally protected much of what now makes up this 63,494-acre preserve, it is now owned by the North Carolina Wildlife Resources Commission, a state government agency created to conserve and sustain the state's fish and wildlife resources. The men had 970 plants in their possession and became the first people charged with a felony for poaching the Venus flytrap. Two of the men were sentenced to 24 months of supervised probation, one was sentenced to 12 months of supervised probation, and the other, who was the only one to not plead guilty, was sentenced to six to 17 months in prison.[2,3]

The Venus flytrap, which can be smaller than a US dime, can be found in Croatan National Forest, on land owned by the North Carolina Division of Parks and Recreation, and on Wildlife Resources Commission game lands in Pender, Brunswick, Onslow, and New Hanover counties.[13] The plant also occurs on several preserves owned by TNC, but the only one of these that is open to the public is the Green Swamp in Brunswick County, according to Crane.

"We've had flytraps poached on our land," Crane told *Scientific American*, adding that thefts of a thousand plants at a time were all too common.[3] "What makes poaching so sad and stupid is that the people who are doing it are local folks," she continued. "They're not making much money off of it. They're selling the bulbs for maybe 25 cents."[3]

Other sources, however, indicate that the poaching can be lucrative.[10,13] Poachers reportedly often sell to out-of-state distributors, and a single plant typically fetches between $7 and $10 at a store.[13]



**Venus flytrap** *Dionaea muscipula*
Photo ©2017 Steven Foster

In the past, the Wildlife Resources Commission made about 10 to 20 arrests per year for poaching on land it controls, but the arrests usually amounted to nothing more than a slap on the wrist before poaching became a felony.[13] "A lot of guys we catch — it's sad to say — it's a family tradition," Sergeant Brandon Dean, of the law enforcement division of the Wildlife Resources Commission, was quoted as saying. "We caught their dad and their dad's dad." Dean also reportedly estimated that one person might be caught for every 200 instances of poaching.[2]

Previously, some offenders continued to poach Venus flytraps even after as many as 20 encounters with law enforcement. The results of poaching could also be seen at depleted and extirpated sites.[10]

According to Dean, when poachers are caught it is often because authorities have been tipped off by other poachers who are protecting "their turf," or by others, such as bird watchers or hikers.[2]

It is too soon to determine whether the stiffer penalties for poaching have helped mitigate the situation. "But [they] certainly [haven't] done any harm," Crane wrote. "The first arrests got lots of attention, which is a good thing."

In *The New York Times*, Dean was quoted as saying, "I would like to think with it being a felony, it put a damper on it. The teeth have definitely been sharpened." He is, however, reportedly doubtful that the poaching will stop completely. He noted that the burden is on enforcers to prove that plants were poached, which is difficult because, according to him, there is no way to distinguish between a plant that was poached from the wild and one that was legally raised in a greenhouse.[2]

However, according to a 2010 *National Geographic* article, the North Carolina Department of Agriculture, at the time, had been dabbing Venus flytraps in the wild with a harmless, invisible dye that glows in ultraviolet light to allow authorities to determine whether flytraps being sold were poached.[14]

Interestingly though, in 2013, Kurup et al. discovered that in the presence of ultraviolet radiation the Venus flytrap (specifically the inside portion of the lobes of the traps) and some other carnivorous species (e.g., pitcher plants in the genus *Nepenthes* [Nepenthaceae]) can attract prey partly by emitting fluorescent blue light that is visible to insects and other arthropods.[15] According to Baby Sabulal, PhD, principal scientist at the Jawaharlal Nehru Tropical Botanic Garden and Research Institute in Kerala, India, and co-author of the study, the Venus flytrap that was analyzed was collected from their garden collection and had not been treated with any dye (email, March 31, 2017). Furthermore, the team consistently found even stronger fluorescent emissions in the *Nepenthes* species that were analyzed, he wrote.



**Venus flytrap** *Dionaea muscipula*
Photo ©2017 Skip Pudney

Conserving the Venus flytrap may also have implications for tourism and, consequently, the economy in North Carolina. "We've had people from all over the world come here to see flytraps," Crane was quoted as saying. "If the plants are gone, [some] tourists are not going to visit."[3]

Also according to Crane, poaching isn't necessary because the plants can easily be cloned (e.g., by cutting). "Flytraps love cloning," Crane was quoted as saying. "You can create them in a greenhouse very easily, and it's being done all over the world. They are being sold legally in a lot of places because they are cloned."[3] The Venus flytrap can also be grown from seed, but it usually takes several years.[16]

According to TNC, there is a good chance that plants sold at a flea market, on the roadside, or online were poached. To help protect Venus flytraps, TNC recommends buying from reputable dealers that do not sell poached stock.[5]

### *Development and Other Threats*

"Poaching is a big problem, but so is development," Crane wrote. Many Venus flytrap habitats have been lost over the last century to development.[3] According to *Dionaea: Venus's Flytrap*, a 2005 follow-up survey of South Carolina Venus flytrap sites found that 70% of the recorded sites had been replaced with golf courses and parking lots.[4]

Protecting flytrap habitats from development and other threats may also have implications for other rare species. One Venus flytrap site was found to support as many as 42 other rare plant species within 25 square meters.[4]

"TNC and the North Carolina Coastal Land Trust have done a lot of work to protect flytrap territory," Crane wrote. "Protecting and restoring habitat is probably more important than efforts focused on poaching." (One expert peer reviewer of this article noted that poached habitat can still feasibly regrow flytraps while paved habitat obviously cannot.)

The mission of the North Carolina Coastal Land Trust is "to enrich the coastal communities of North Carolina through conservation of natural areas and working landscapes, education, and the promotion of good land stewardship," according to its website.[17] It has become the largest land trust, geographically, in the state, and it is qualified to accept and hold conservation agreements. Landowners who are interested in protecting their land from development may choose to enter into a conservation agreement with a qualified conservation organization or government body. This legally binding agreement



"American Bog Plants." Illustration from *New Illustration of the Sexual System of Carolus von Linnaeus* by Robert John Thorton (1768-1837)
Image courtesy of Botanicus.org



permanently limits the uses of all or part of a property in exchange for tax savings, charitable contributions deductions, income tax credits, and lower property taxes for the landowner.[18]

The Coastal Land Trust holds conservation agreements on two properties with flytraps. In addition, it has purchased in fee title three properties with flytraps; it owns and manages two of these as nature preserves, and it transferred the other (which abuts part of the Croatan National Forest) to the Wildlife Resources Commission to be managed as game land (email from Janice Allen, deputy director of the Coastal Land Trust, April 3, 2017).

Although many of the remaining known Venus flytraps occur on protected lands, development is still a significant concern for at least two reasons, according to Crane. First, TNC, which manages preserves in all 50 US states and has protected more than 700,000 acres in North Carolina alone (from the Outer Banks to the Southern Blue Ridge Mountains),[19] suspects the plants also occur on some unprotected private lands because those lands are similar to the public lands where the plants are known to occur. "If those lands are developed, then the plants [that TNC suspects grow there] will be lost as well," she wrote. Second, "development can have a negative effect on nearby lands that may already be protected by draining them, causing runoff, or preventing the use of fire to restore land. When you have neighborhoods close by, it is really hard to put controlled burns on the ground."

Fire is particularly important for the Venus flytrap. Without it, shrubs take over and shade out the sun-loving plants, which need an open understory (the layer of vegetation, especially the trees and shrubs, between the canopy and the ground cover) to survive. Fire suppression may help protect human developments, but it has affected large swathes of land that Venus flytraps inhabit, including the Green Swamp. TNC is working to restore these habitats through controlled, or prescribed, burns that mimic natural fires.[5,6]

Fire suppression may help protect human developments, but it has affected large swathes of land that Venus flytraps inhabit, including the Green Swamp. The Nature Conservancy is working to restore these habitats through controlled, or prescribed, burns that mimic natural fires.

"We do use controlled burning to manage habitat for flytraps and other plants," Crane wrote. "Ideally, the fires should be put on the land in a regular interval."

There is evidence that with a fire return interval (i.e., the time between fires in a specified area) of more than five years, Venus flytrap populations decline precipitously. In addition, some data show that the largest and densest remaining flytrap populations occur in places with the longest and most regular history of burning.[4]*

In the future, rising sea levels may also pose a concern. "[Venus flytraps] only occur in low-lying areas near the coast, so, yes, over time, sea level rise will likely affect them," Crane wrote.†

Changing soil fertility may also affect the Venus flytrap. The soil of bogs typically contains little nitrogen and phosphorus. So, the Venus flytrap, like other carnivorous plants, has adapted to obtain these nutrients in other ways, thereby compensating for the deficiencies of the soil. However, pollution from power plants and agricultural runoff has added extra nitrogen to many bogs in North America, and this can prove fatal to carnivorous plants, presumably including the Venus flytrap, which are attuned to low levels of nitrogen.[14]

### *Conservation Status and Regulations*

The Venus flytrap is considered vulnerable‡ according to the Red List criteria of the International Union for Conservation of Nature (IUCN).[20] Version 3.1 of the *Red List Categories and Criteria* states that a taxon is vulnerable "when the best available evidence indicates that it meets" at least one of the listed criteria, "and it is therefore considered to be facing a high risk of extinction in the wild."[21] The Venus flytrap was among 250 rare and threatened species included in the first IUCN *Plant Red Data Book*, published in 1978. The publication arose from pioneering work by botanists at the Herbarium at the Royal Botanic Gardens, Kew, in England, who recognized that the plights of many plant species in danger of extinction were less publicized than the plights of some rare and charismatic animals.[8]

The IUCN's *Red List of Threatened Species* is the world's most comprehensive information source on the conservation status of plant, animal, and fungal species. The *Red List Categories and Criteria* provides an explicit, objective framework for classifying species at high risk of global extinction, based on parameters such as population reduction and restricted geographic range.[22]



**Venus flytrap** *Dionaea muscipula*
Photo ©2017 Calyponte

The Venus flytrap is also currently listed in Appendix II of the Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES).[23] CITES, which came into effect in 1975, is an international agreement intended to ensure that international trade of certain animal and plant species does not threaten the survival of those species. Currently, 183 countries, or Parties, including the United States, have voluntarily agreed to adhere to the Convention. CITES is legally binding for the Parties, but it does not take the place of national laws. Instead, each Party must adopt domestic legislation to ensure that CITES is implemented at the national level.[24] Currently, more than 35,000 species of animals and plants, including the Venus flytrap, are listed among the three CITES appendices, which afford varying degrees of protection.[24-25]

Appendix II includes species that are not necessarily threatened with extinction but for which trade must be controlled to avoid overexploitation. For these species, including the Venus flytrap, "an export permit or re-export certificate issued by the Management Authority of the State of export or re-export is required. An export permit may be issued only if the specimen was legally obtained and if the export will not be detrimental to the survival of the species. A re-export certificate may be issued only if the specimen was imported in accordance with the Convention." However, import permits are not needed for species listed in Appendix II "unless required by national law."[25]



**Venus flytrap** *Dionaea muscipula*
Photo ©2017 Steven Foster

In October 2016, a petition filed with the Secretary of the Interior requested the United States Fish and Wildlife Service (USFWS) to immediately protect the Venus flytrap as a recognized endangered species under the Endangered Species Act (ESA) of 1973.** The ESA states that a species shall be determined to be endangered or threatened based on any of five factors, and the petitioners wrote that the Venus flytrap is threatened by at least four of those factors (i.e., curtailment of habitat, overutilization, inadequacy of existing regulatory mechanisms, and other natural or manmade factors). "The decision by the [USFWS] not to list the Venus Flytrap as Threatened or Endangered in 1993 has led to continuing declines in its range and abundance since then," the petitioners wrote.[27]

Benefits for plants and animals that are listed as endangered or threatened under the ESA include the following: protection from being jeopardized by federal activities, protection from having critical habitat destroyed or adversely modified, restrictions on take and trade, a requirement that the USFWS develop and implement recovery plans for listed species under US jurisdiction, authorization to seek land purchases or exchanges for important habitat, and federal aid to state and commonwealth conservation departments with cooperative endangered species agreements. Listing can also encourage conservation efforts by other agencies, independent organizations, and individuals.[28]

"We have reached a situation in which there are more flytraps

* One expert peer reviewer of this article noted that "the best wild populations from my experience occurred on military lands that burned from regularly exploding ordinance."

† According to a peer reviewer of this article, sea level rise is not an immediate threat to the Venus flytrap. The reviewer created a geographic information system (GIS) model in 2016 and found that the lowest elevation sites with Venus flytraps were 26 feet above sea level.

‡ The current conservation assessment for the Venus flytrap found on the IUCN Red List website was published in 2000 and used the previous version (Version 2.3) of the IUCN *Red List Categories and Criteria*. According to one expert peer reviewer of this article, a reassessment is needed. "This is not to predict that the category assigned (vulnerable) will be different, but the criteria used will be more relevant to the data available," the reviewer wrote.

** Though the law establishes a two-year timeline for species to be listed under the ESA, a 2016 study found that it takes, on average, 12.1 years for a species to be listed. Some species went through the process in six months, but some species, including many flowering plants, took 38 years to be listed (most of the history of the ESA).[26]

in captivity than in the wild," Donald Waller, PhD, a professor of botany at the University of Wisconsin-Madison who co-authored and signed the petition, was quoted as saying. "That might be construed as good news, if it assures they will survive in captivity, but it's distressing for ecologists and conservation biologists. A population can only persist and evolve in its native habitat, and we've already seen the disappearance of 90 percent of wild plants. We have lost whole bogs, populations and individuals."[29]

## Medicinal Properties of the Venus Flytrap

The Venus flytrap contains compounds that can benefit human health, including naphthoquinones, phenolic acids, and flavonoids.[30]

According to a 2013 review by Gaascht et al., more than 15 compounds have been isolated from the Venus flytrap, although most of these are also found in other plants. At the time of the review, only one compound thought to be unique to the Venus flytrap with medicinal potential had been isolated: diomuscipulone. This naphthoquinone, however, has apparently not been tested for its biological activity.[30]

Many of the compounds found in the Venus flytrap, including the naphthoquinone plumbagin (also present in *Plumbago zeylanica* [Plumbaginaceae] and other plants) and the phenolic acids ellagic acid (also present in pomegranate [*Punica granatum*, Lythraceae] and many other plants) and salicylic acid (also present in *Salix* spp. [Salicaceae]), have been shown to modulate the NF-κB cell-signaling pathway. This may be significant because this pathway is involved in the development and progression of many types of cancers.[30]

Several of the compounds found in the Venus flytrap, including salicylic acid and the flavonoids quercetin and kaempferol (which are both present in *Ginkgo biloba* [Ginkgoaceae] and many other plants), have been the subjects of pharmacokinetic studies and clinical trials. Though most studies show that these compounds have poor bioavailability, it has been shown that co-treatment with a natural compound like quercetin or kaempferol and a chemotherapeutic drug like cisplatin or etoposide is more efficient than a single treatment, probably because of the ability of the natural compounds to block a specific drug resistance mechanism used by cancer cells.[30]

Plumbagin may be one of the most promising anticancer compounds present in the Venus flytrap.[30] It has demonstrated anticancer and antiproliferative activities in animal models and cell cultures and has been shown to target a wide range of cancer types, including breast cancer, lung cancer, ovarian cancer, acute promyelocytic leukemia, and prostate cancer.[31]

In addition, plumbagin and its derivatives appear to have antibacterial properties. A 2013 in vitro study showed that the plumbagin derivatives maritinone and 3,3'-biplumbagin (isolated from a plant other than the Venus flytrap) were 32 times more potent than the antimycobacterial drug rifampicin against a strain of *Mycobacterium tuberculosis* that was pan-resistant (i.e., resistant to all five first-line anti-tuberculosis drugs). The authors concluded that these two derivatives have the potential for development as new anti-tuberculosis drugs, especially against resistant strains.[32]

In the 1970s, the German physician Helmut Keller, MD, observed a Venus flytrap while in a flower shop in Maine and wondered if the plant contained substances that could be used selectively against tumor cells. He eventually developed a patented extract of the Venus flytrap called Carnivora.[33] Although some anecdotal evidence suggests that Carnivora may be an effective cancer therapy,[34] it does not appear to have been the subject of any human clinical trials. According to the Carnivora website, its manufacturing process does not use any Venus flytraps from wild habitats.[35]

Daniel Moerman's *Native American Ethnobotany*, a highly respected compilation of the ethnobotanical uses of North American plants by Native American peoples, does not indicate that the Venus flytrap was used medicinally by Native Americans, but it does state that the Cherokee used a "small piece of plant chewed and spat on bait for fishing."[36]

Although the Venus flytrap does not seem to be a major part of the commercial herb trade, the plant does contain compounds with demonstrated anticancer effects and other potentially beneficial biological activities.

## Botany and History of the Venus Flytrap

The Venus flytrap is an herbaceous perennial that, from a rhizome, produces a low-growing rosette (which can be five inches tall and eight inches wide) of up to eight or more bristly, spreading, basal leaves (traps) that can each be five inches long. White flowers bloom in spring, from about May to June, on leafless stems that rise above the foliage up to about one foot tall.[16]

The plant belongs to a monotypic genus (i.e., it is the only species in the genus *Dionaea*). It is closely related to the waterwheel plant (*Aldrovanda vesiculosa*), which also belongs to a monotypic genus in the Droseraceae family (though there are extinct *Aldrovanda* species).[8] The waterwheel plant is a rootless, free-floating, freshwater carnivorous plant that consumes aquatic invertebrates and has been called the "aquatic sister" of the Venus flytrap. Unlike the Venus flytrap, the waterwheel plant is considered endangered according to IUCN Red List criteria because, even though it is widely distributed geographically, it has declined over the last century to only 50 confirmed extant locations.[37]

Phylogenetic analysis based on DNA sequence data has shown that the Venus flytrap and the waterwheel plant, which are the only known snap traps (a kind of active trap), are descended from a common sticky "flypaper" trap ancestor (i.e., one that captures prey using a sticky mucilage). This ancestor would have been in the Droseraceae family and would have been similar to sundew (*Drosera*) species, but it is presumed extinct. According to Gibson et al., the snap traps adapted to catch and retain larger prey, resulting in disproportionate rewards, compared to the sticky traps, which allow larger prey to escape. It has also been shown that the king sundew (*Drosera regia*, Droseraceae), a flypaper trap, is the closest known living relative of the two snap traps.[38]

Because there is some disagreement in the scientific community about what exactly constitutes carnivory in plants, there is also disagreement about how many carnivorous plant species there are. For example, in 2009, Chase et al. proposed that some species not widely considered to be carnivores, such as species in the genus *Stylidium* (Stylidiaceae), and some species in the genera *Potentilla* (Rosaceae), *Proboscidea* (Martyniaceae), and *Geranium* (Geraniaceae), are just as carnivorous as other carnivorous species.[39]

Regardless of how many carnivorous plant species there are, and most sources indicate there are more than 600, the Venus flytrap may be the most famous of them all, probably largely because of its ability to snap shut so quickly.[40] Other active traps use mechanisms that are different from the two snap traps to capture prey. For example, aquatic bladderwort species (i.e., aquatic species in the genus *Utricularia* [Lentibulariaceae]) pump water out of the bladder of the plant, which decreases pressure inside the bladder and creates a vacuum that rapidly sucks prey in to be digested when the trapdoor is triggered to open even slightly.[38,41] By even greater contrast to the snap traps, pitcher plants (species in the genera *Sarracenia* [Sarraceniaceae], *Nepenthes*, and others), for example, are passive traps (specifically pitfall traps) that use nectar to lure prey to slip into the trap.[41] Thus, the snap traps are unique, and this uniqueness is likely responsible for the Venus flytrap's popularity.

The Venus flytrap's Latin binomial *Dionaea muscipula* originated from a published letter, dated September 1, 1768, by English naturalist John Ellis, who credited the genus name to Swedish naturalist Daniel Solander. Ellis wrote: "At the request of Mr. Collinson, the ingenious Dr. Solander … dissected this plant before some of his friends; and from the beautiful appearance of its milk-white flowers, and the elegance of its leaves, thought it well deserved one of the names of the goddess of Beauty, and therefore called it *Dionaea*…. I shall only add a specific name to distinguish it from others of this genus, that may possibly be discovered hereafter. From the structure then and particular moving quality of its leaves when irritated, I shall call it *Dionaea Muscipula*, which



**Venus flytrap** *Dionaea muscipula*
Photo ©2017 Mark Goddard

may be construed into English…either Venus's Flytrap or Venus's Mousetrap."[42] In Greek Mythology, Dione is the mother of Aphrodite, the goddess of love and beauty, whose Roman counterpart is Venus. In Latin, "muscipula" means mousetrap.

Ellis later sent a letter, dated September 23, 1769, to Swedish botanist and "Father of Modern Taxonomy" Carl Linnaeus, in which he described the Venus flytrap. Ellis also enclosed a picture of the plant with his letter.[43] Linnaeus described the plant as a "miraculum naturae,"[39] but apparently rejected the idea that a plant could consume an animal, saying that would go "against the order of nature as willed by God." He reasoned that the sensitive plants capture animals only by accident, and that once a captured animal stopped struggling, it would be released.[14]

In his book *Travels*, published in 1791, American naturalist William Bartram, the son of botanist John Bartram, wrote the following of the Venus flytrap: "Astonishing production! See the incarnate lobes expanding, how gay and ludicrous they appear! Ready on the spring to intrap incautious deluded insects, what artifice! There behold one of the leaves just closed upon a struggling fly, another has got a worm, its hold is sure, its prey can never escape—carnivorous vegetable! Can we after viewing this object, hesitate a moment to confess, that vegetable beings are imbued with some sensible faculties or attributes, similar to those that dignify animal nature; they are organical, living, and self-moving bodies, for we see here, in this plant, motion and volition."[7,44]

Years later, Darwin also knew better than Linnaeus, but even he could not imagine some of the plant's abilities before observing a specimen for himself. In a letter to English botanist Daniel Oliver, dated September 11, 1860, Darwin wrote: "Lastly would you look at the *Dionaea* (if you have living specimen) and observe whether the hairs are viscid, for it almost passes my belief that the leaf can snap so quick as to catch a fly, unless it be in some degree entangled…."[45]

Darwin later learned differently, and, in *Insectivorous Plants*, wrote: "the sensitive filaments of *Dionaea* are not viscid, and the capture of insects can be assured only by their sensitiveness to a momentary touch, followed by the rapid closure of the lobes."[1]

## The No-Fly Zone: How the Venus Flytrap Catches and Digests Prey

The Venus flytrap uses sweet-smelling nectar to lure prey into its traps.[16] There are between three and six trigger hairs (trichomes) on the inside surface of each lobe of each trap.[46] Presumably to prevent the plant from wasting energy by responding to non-prey stimuli, such as raindrops and dust, the trap will close only when one hair is touched twice or two hairs are touched within about 20 seconds. This indicates that the plant can remember the first electrical signal for a short time.[47] If a second signal is not received within about 20 seconds, the process resets, but if it is, the cells on the outer surface of the leaf expand rapidly and the trap shuts almost instantly (in about 100 milliseconds; for comparison, the waterwheel plant can shut in about 10 milliseconds), and snaps from convex to concave.[46,47] This type of movement is called thigmonasty (a non-directional response to being touched).[6]

More than three flicks of a trigger hair are necessary for the plant to begin to secrete the digestive enzymes that dissolve its prey. When the trapped prey struggles, it trips the trigger hairs repeatedly, and this struggle gives the plant a way to judge the amount of digestive enzymes needed, and thereby save energy. More electrical signals from the trigger hairs being tripped seems to correlate proportionally with more digestive enzymes being secreted.[47] The nutrients from the prey are absorbed and, after five to 12 days, the trap reopens to release the leftover exoskeleton.[46]

While larger Venus flytrap plants produce larger traps, it has been shown that the number of traps per plant actually remains steady or even decreases as the plants grow larger. Smaller traps on smaller plants seem specialized for catching smaller prey, especially ants, and larger traps often catch spiders and beetles.[38]

After three to five meals, a leaf will no longer capture prey but will exclusively photosynthesize for about two to three months before it falls off the plant. After about 10 unsuccessful closures, a trap will no longer respond to touch and will only photosynthesize.[46] It has been estimated that a Venus flytrap can live up to 20 years, or possibly longer.[6]

**Venus flytrap** *Dionaea muscipula*. Photo ©2017 Joe MiGo



## Conclusion

The Venus flytrap is a sophisticated, one-of-a-kind plant, but, ironically, it is the sophisticated adaptations that this plant has developed to survive and thrive that have led to the poaching that is now one of the main threats to the plant's survival in the wild.

According to Waller, who co-authored the petition to give the flytrap protection under the ESA, wild populations can be protected without reducing demand for the plant. "Let's encourage [demand]," he wrote (email, March 30, 2017). "Flytraps can be easily propagated. But we do need to shut down poaching of plants from the few remaining wild populations. So why not give consumers a way to satisfy their demand for this plant by buying certified propagated plants? While we are at this, let's ask for 50 cents or $1 per plant to protect and maintain wild habitats. Most of us would appreciate the chance to protect wild populations while indulging our passion for this plant."

Waller also thinks that potential habitats for this species need protection from development and other threats. "Especially the larger blocks of habitat that work effectively to sustain regular new colonizations," he wrote. "Second, these areas need active management if they are to function as habitat for the flytrap. In particular, we must sustain their hydrologic and fire regimes. In other words, we need to make sure they stay wet and burn regularly. Flytraps need sun and water, but they lose these when shrubs overgrow their habitats or people drain swamps and savannas."

Flytrap habitats, however, cannot be burned every year or all at the same time, according to Waller. "Burning various patches of habitat in alternation with each other allows a steady stream of new favorable patches to colonize," he wrote.

"This plant charms us all," Waller wrote. "Carnivorous plants are all fascinating, but this plant is the most fascinating of all. It is also the sole terrestrial representative of a remarkable evolutionary event — the evolution of a rapidly closing snap trap." HG

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**Venus flytrap** *Dionaea muscipula*
Photo ©2017 Che (Wikicommons)

***DIY Bitters: Reviving the Forgotten Flavor — A Guide to Making Your Own Bitters for Bartenders, Cocktail Enthusiasts, Herbalists, and More*** by Guido Masé and Jovial King. Beverly, MA: Fair Winds Press, Quarto Publishing; 2016. Hardcover; 208 pages. ISBN: 978-1-59233-704-0. $24.99.




Guido Masé and Jovial King, the chief herbalist and founder, respectively, of Urban Moonshine in Burlington, Vermont, have teamed up to produce an essential book on herbal bitters. The "DIY" in the title, for those unfamiliar with the trend, stands for "Do It Yourself," which readers surely will after reading this guide and understanding the health-promoting attributes of bitter agents in the diet.

This beautifully illustrated and well-organized work begins by presenting basic and non-technical information about the sense of taste and its relationship to the mouth and gut, indicating how the bitter component of human diets has been relegated to poor stepsister status in a world that worships sugar, fat, and salt, much to the detriment of body mass indices and overall health. Our ancestors generally had a prominent intake of bitter plants that helped curb excess feasting, maintain a healthy body weight, and provide important phytonutrients, but agricultural worship of the more "palatable" vegetables and the widespread predominance of empty calories in the modern diet have proven detrimental, wreaked havoc on blood sugar levels, and contributed to increases in autoimmune diseases.

Returning bitters to the diet may help reverse these trends. The reader will learn that the world of bitters is populated with a wide cast of herbal characters and biochemicals, including flavonoids and polyphenols with antioxidant and anticancer effects; triterpenes with immune-regulatory benefits; organic acids like those in chicory (*Cichorium intybus*, Asteraceae) that improve glucose balance and regulate appetite; lactones from dandelion (*Taraxacum officinale*, Asteraceae) that detoxify the system; iridoids like those from gentian (*Gentiana lutea*, Gentianaceae) that combat heartburn, decrease sugar craving and promote digestion; alkaloids like quinine in cinchona (*Cinchona* spp., Rubiaceae) with myriad pharmacological therapeutic benefits; and complex polysaccharides, such as those in burdock (*Arctium lappa*, Asteraceae) that act as prebiotic feedstocks for beneficial probiotic bacteria that are essential for proper digestion, endocannabinoid tone, and optimal health.[1]

Anyone who has had the pleasure of hearing Masé lecture or reading his previous book will know that he is a great herbal historian and storyteller, and that talent is displayed nicely in this text.[2] Each plant receives an engaging account of its background and history of use by humans. As a DIY treatise, proper attention is given to tools of the tincturing trade and best strategies to produce a formidable home arsenal of bitters for every occasion.

The book proceeds to a rogues' gallery of bitter herbs, organized alphabetically by common name from agrimony (*Agrimonia eupatoria*, Rosaceae) to yellow dock (*Rumex crispus*, Polygonaceae), with a description of traditional use, plant part(s) employed, flavor, chemical contribution, extraction strategy, and a recipe suggestion. One notable outlier is certainly not kosher, as the smoked and cured *Sus scrofa domesticus* flesh is required if the carnivorous among us wish to avail themselves of "Bacon Bitters."

*DIY Bitters* features 60 enticing recipes that are not merely confined to tinctures. Examples include the following: "Coffee Cutter," a mixture of roasted burdock, chicory, and dandelion roots meant to enhance the flavor of coffee (*Coffea arabica*, Rubiaceae); "Barolo Chinato," an Italian amaro created by adding a host of herbs to a fine vintage; "Bitter Melon Chutney," a side dish made with *Momordica charantia* (Cucurbitaceae); "Kava-Ginger Pastilles," spicy candies made with *Piper methysticum* (Piperaceae) and *Zingiber officinale* (Zingiberaceae); and "Iron Tonic Syrup," a nourishing blend of various herbs and molasses.

These are accompanied by recipes for the more traditional "Angostura" bitters and "Bloody Mary Bitters" to buffer or better the taste of alcohol in a cocktail, along with seasonal recipes for optimizing health with fresh herbs of the moment, and symptom-specific recipes for sleep, dreaming, fever, and liver and immunological support. Several celebrity selections from Tieraona Low Dog, MD; Jim McDonald; Christopher Hobbs, PhD, LAc; and Rosemary Gladstar are certain to encourage lucky readers to try their hands at recipes shared by these herbal luminaries.

The book displays large font and lovely phyto-photography, and so represents the perfect gift solution for the herbally oriented person with advancing presbyopia and an expanding waistline. It would be an outstanding companion volume to the recent culinary offering on the subject.[3] *DIY Bitters* deserves an honored place in the library of every gardener and herbalist as they consider projects to optimize health with the aid of nature's harvest. HG

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**Los Angeles, California**

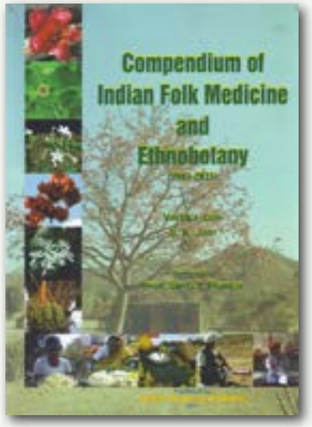
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***Compendium of Indian Folk Medicine and Ethnobotany (1991-2015)*** by Vartika Jain and S.K. Jain. New Delhi, India: Deep Publications; 2016. Hardcover, 542 pages. ISBN: 978-93-80702-10-0. $125.00.




India has something unique that I wish we had here in the United States: a central government Ministry of Ayurveda, Yoga & Naturopathy, Unani, Siddha and Homoeopathy (AYUSH). Besides a mandate of standards for education, clinical practice, and research for the codified and scholarly Indian systems of medicine, the scope of the Ministry of AYUSH includes research into India's extensive non-codified oral traditions that stem from regional, tribal, and folk medicines. Concerning the latter, this new work makes a considerable contribution to the ethnobotanical literature and, in particular, to the awareness of India's rich heritage of indigenous medical knowledge.

This well-referenced, 542-page compendium was compiled by Vartika Jain (VJ), PhD, of the department of botany at the Government Meera Girls College in Udaipur, Rajasthan, and the now-90-year-old Sudhanshu Kumar Jain (SKJ), PhD, former director of the Botanical Survey of India and founder-director of the S.K. Jain Institute of Ethnobiology in Lucknow, Uttar Pradesh. The reason that a specific 25-year period (1991-2015) is provided parenthetically as part of the book title is because this work is a sequel to SKJ's 1991 book, *Dictionary of Indian Folk Medicine and Ethnobotany: A Reference Manual of Man-Plant Relationships, Ethnic Groups & Ethnobotanists in India* (Deep Publications, 1991). While the 1991 dictionary covered 2,532 plant species, this 2016 compendium provides ethnobotanical data on a total of 4,663 plant species. Of the 1,000 references cited in this book, 246 of them are tribe-specific and cover 141 tribal groups. (There are, however, more than 700 different tribal and other distinct ethnic communities in India.) Sixty-six references are single genus/species-specific, and nine are botanical family-specific.

Organized like an encyclopedia, the 4,663 different species are listed by Latin binomial in alphabetical order. The authors mainly relied on two authoritative sources for nomenclature of angiosperms, gymnosperms, pteridophytes, and bryophytes of the plant kingdom: The Plant List (a collaboration between the Royal Botanic Gardens, Kew, and the Missouri Botanical Garden) and the Tropicos database (Missouri Botanical Garden). For nomenclature of fungi and lichens, the authors used the MycoBank database (International Mycological Association) and for algae, the AlgaeBase database (National University of Ireland) was accessed. If the authors were uncertain of the identity of a species (and in the absence of voucher specimens), the name is qualified with a question mark in parentheses.

For brevity, due to the already large size of this book, abbreviations are used throughout for plant parts (e.g., rb = root-bark), names of diseases (e.g., malar = malaria), indications for use (e.g., flatu = flatulence), pharmacological action (e.g., galact = galactagogue), ethnobotanical use categories (e.g., Med = medicine; Ed = Edible; and Symb = symbolic), and zones of India where the plant is used (e.g., zone A = Jammu & Kashmir [JK] and Himachal Pradesh [HP]). Fortunately, the footer at the bottom of each two-page spread provides abbreviations for the plant parts and the eight designated regions of India. Until one memorizes all of the other abbreviations used, there will be some paging back and forth to the lists of abbreviations. Each abbreviated listing also includes the numeric reference, which is very helpful.

To illustrate, some selected uses for *Moringa oleifera* (Moringaceae) are described in the text as follows: "Med galact (lf 377 F; lf 952 F)," which means that the leaf is used in folk medicine as a galactagogue in region F — Madhya Pradesh (MP), Maharashtra (MH), and Andhra Pradesh (AP) — supported by references 377 and 952; "musical instrument tambura (wd 532 B; wd 533 B)," which means that the wood of the tree is used to make tamburas in region B — Punjab (PB), Haryana (HAR), Rajasthan (RAJ), and Gujarat (GUJ) — supported by references 532 and 533; "Symb. bk spread in house to ward off snake (3 D)," which means that the tree bark is used symbolically to keep snakes out of the house in region D — Bengal (BENG), Bihar (BI), Jharkhand (JHA), Chhattisgarh (CHH), Orissa (ORI), and Sikkim (SKM) — supported by reference 3.

One set of data that may be lacking in this work relates to the geographical origin of the listed species. Given that this is a compendium of folk medicinal and ethnobotanical uses by tribes in India, one could easily make an (incorrect) assumption that the 4,663 listed species are also native to India (and therefore part of the traditional ecological and medical knowledge of India). The listings do not provide information as to whether a species is native to India or introduced, naturalized, escaped from cultivation, and/or invasive. I was initially surprised to find listings for several native American plant species, including papaya (*Carica papaya*, Caricaceae), California poppy (*Eschscholzia californica*, Papaveraceae), passionflower (*Passiflora incarnata*, Passifloraceae), chocolate (*Theobroma cacao*, Malvaceae), and corn (*Zea mays,* Poaceae), among others.

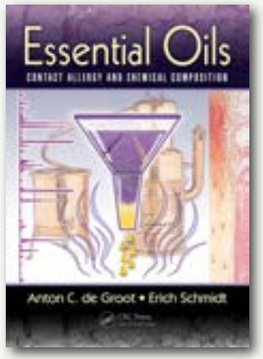
Digging deeper, I found that many species native to the Americas (North and South), as well as to Europe and the Mediterranean region, are included in this work. That is

not to say that introduced species cannot have legitimate folk medicine uses in a new country, but only to say that these would be relatively new, as opposed to ancient, uses. Many plants have been transported and have adapted to new ecosystems, especially during the European colonial period.

I will be making good use of this compendium and can recommend it, as the authors do, to anthropologists, botanists, historians, linguists, nature conservationists, and those engaged in phytopharmaceutical research. As a researcher of botanical nomenclature, I greatly appreciate (and will make use of) this book's "Index to Local Names," which covers 179 pages and contains more than 21,000 local plant names with their corresponding Latin binomial. In the future, when colleagues contact me by Skype, they will see this book on a shelf right behind me where I can easily reach it when carrying out desk research. HG

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**Traditional Medicinals**
**Sebastopol, California**

***Essential Oils: Contact Allergy and Chemical Composition*** by Anton C. de Groot and Erich Schmidt. Boca Raton, FL: CRC Press; 2016. Hardcover, 1058 pages. ISBN: 978-1482246407. $199.95.




At last, serious and reliable scientific books about essential oils have started to appear in the market. *The Handbook of Essential Oils: Science, Technology and Applications* has been published in two editions (2010, 2016) in the last six years. I consider *Essential Oils: Contact Allergy and Chemical Composition*, with its 1,000-plus A4-size pages, to be complementary.

Anton C. de Groot, PhD, is a dermatologist with a special interest in contact allergies. Erich Schmidt is an industry-based essential oil specialist. Their joint efforts have given rise to a comprehensive book on essential oils with particular emphasis on allergic reactions. Scanning the literature, they have identified 79 essential oils with a record of contact dermatitis and compiled chemical data and allergy information about 93 materials (91 essential oils and two absolutes). The book lists 4,350 chemical substances found in those oils and treats them critically with proper literature references. Such comprehensive information is difficult to find in a single book. Therefore, it will be a valuable source for essential oil researchers.

The introductory chapters on essential oils are short but informative, and provide the basics while emphasizing the correct terminology, which is necessary. Contact allergy and allergic contact dermatitis are discussed in general, and specific, related information is provided for each oil and absolute. All the essential oils and absolutes mentioned in the book are traded and used by food, cosmetics, pharmaceutical, and perfumery industries.

Chapter 5 comprises individual monographs on each of the 93 products. Each monograph contains a definition, source information (plant species and part yielding the oil), INCI (International Nomenclature of Cosmetic Ingredients) name, CAS (Chemical Abstracts Service) registry number, EINECS (European Inventory of Existing Commercial Chemical Substances) number, ISO (International Organization for Standardization) information, chemical information, uses, and chemotypes (if any). Contact dermatitis/allergy data are provided in brief, and known constituents of the oil are listed in tabulated form complete with footnotes and references. Major constituents are listed with percentage limits in a separate table. These lists contain information extracted from literature as well as Erich Schmidt's personal unpublished data.

In Chapter 6, compounds found in essential oils are listed alphabetically with reference to related oils in which the compounds have been identified. Chapter 7 contains synonyms of the listed compounds, and the book ends with an index.

The only thing I may criticize is that 26 substances that are restricted in the European Union have not been covered, even briefly. Most of those volatile substances, such as methyleugenol, pulegone, alpha- and beta-thujone, coumarin, estragole (methylchavicol), menthofuran, beta-asarone, and safrole, frequently are found in essential oils. Reference to those compounds in the book could have been useful to the general reader, since the compounds often are the subject of toxicological concern.

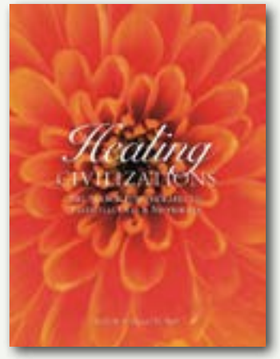
The book is a useful source of information on essential oils. I recommend it to all those interested in essential oils, and in particular to dermatologists, nurses, and other health care professionals; students, workers, and experts in food, agriculture, pharmacy, cosmetics, and perfumery sectors; and aromatherapists. HG

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**Department of Pharmacognosy**
**Nicosia, Northern Cyprus**





***Healing Civilizations: The Search for Therapeutic Essential Oils and Nutrients*** by Nadim Shaath. Petaluma, CA: Cameron and Company; 2017. Hardcover, 321 pages. ISBN: 9781944903091. $65.00.




Seven years in the making, this large coffee-table-style hardcover book is the culmination of the world travels of Nadim Shaath, PhD, over 25 years, and it is as beautiful as it is informative. Shaath scoured the globe in search of remedies and healing traditions, and investigated a wide variety of sources, from ancient writings, early pharmacopeias, and ancient civilizations to modern-day ingredients and practices. Traveling across continents, Shaath met with scientists, industrialists, farmers, healers, and historians to chronicle discoveries both past and present. Dozens of ingredients were analyzed and catalogued into practical information relevant to herbal and aromatherapy practitioners, perfumers, researchers, and complementary care providers. Award-winning photojournalist Thomas Hartwell contributed gorgeous color photos on nearly every page, which helps transport the reader to these lands that are so rich in history and healing traditions.

With an emphasis on environmentalism and a plea to return to the roots of healing, Shaath encourages the reader to partake cautiously of modern pharmaceuticals and reconsider the overreliance on synthetic ingredients, products, and drugs. Acknowledging the advances in modern medicine to increase longevity, he notes that the contributions to natural healing by early civilizations must be remembered, and implores readers to consider these earth-friendly remedies with tested performance over centuries of safe and (ostensibly) effective use.

Shaath places an emphasis on his native country, Egypt, mining its golden history of scientific knowledge that is unequalled. He references information carved on temple walls and papyrus scrolls, which list plants that are used for everything from cosmetics to medicines. Many of these plants are used for similar purposes to this day. Exploratory travels took him to other lands, including Israel, Turkey, France, Italy, Greece, Spain, Morocco, India, Asia, South Africa, the Americas, and more. The author discusses the impact of each of these locations on the development of modern holistic and homeopathic remedies, and the therapeutic uses of botanical ingredients, including both herbs and essential oils.

This book walks readers through the progression of humanity, and includes lessons from past botanical knowledge that can be applied in the future. It is composed of 16 chapters, an extensive list of references, and a well-organized index. The chapters are: "Historical Perspectives"; "The Call to Naturals"; "Egypt"; "The Silk Road"; "Europe"; "The New World and the Americas"; "Ancient Egyptian Cosmetics, Toiletries and Therapeutic Ingredients"; "The Influence of Ancient Practice on Today's Modern Therapy"; "The Production of Essential Oils and Absolutes"; "Essential Oils and Absolutes" (a materia medica of Shaath's personal favorites); "Fixed Oils and Therapeutic Nutrients"; "The Art of Perfumery"; "Medical Aromatherapy"; "Quality Control and Analytical Methods"; "Templates of 50 Essential Oils and Absolutes"; "Templates of 20 Fixed Oils and Therapeutic Ingredients." There is also an epilogue, titled "Where Are We Headed Now?," which notes that although many aromatherapy and herbal preparations are now mainstreamed into complementary care, more studies are needed to substantiate ancient wisdom and provide integrative care that will allow us to achieve healthy living.

An extra note about Chapter 15: It encompasses a large portion of this book (102 pages) and provides everything that a quality evaluator needs to characterize the 50 listed essential oils, which were chosen for their historic context, current popularity, and modern commercial uses. The easy-to-read two-page template for each oil includes 13 parameters: product identification; physiochemical properties; gas chromatography results; regulatory status; safety data; country of origin; price scale; perfumery scale; aromatherapy properties; stability; storage conditions; historical/folk traditional uses; and mass spectrometry evaluation (of the active/main component). This information comes from Shaath's extensive personal experience. The section on fixed oils is similarly informative.

This book is an homage to natural ingredients across the globe with a plea to return to clean and green ingredients in foods, medicines, and cosmetics. Shaath concludes that ancient remedies are still effective options that support the health of the planet and its inhabitants.

The book provides brief descriptions of some ancient remedies, and includes appropriate cautions for responsible use. It also has a few aromatherapy blend suggestions and skin-care applications, but it is not a formulary book. *Healing Civilizations* is punctuated with interesting historical anecdotes, mythologies, and extensive narratives about the lore of many of these ingredients, making this book more than a reference, but also a captivating read. Though the historical information is fascinating, the greatest contribution to an essential oil library or professional laboratory is the extensive and informative reviews of the 50 essential oils and the fixed carrier oils. The book compiles a host of regulatory information that is invaluable to anyone working in the natural products industry in general, and in personal care specifically. Although the book contains a few very minor errors, I recommend it to anyone from beginners to advanced users of botanical ingredients, especially those with an interest in the historical roots of herbalism. HG

**—Mindy Green, MS, RA, RH (AHG)**
**www.greenscentsations.com**




***The Good Living Guide to Natural and Herbal Remedies: Simple Salves, Teas, Tinctures, and More*** by Katolen Yardley. New York, NY: Skyhorse Publishing; 2016. ISBN: 9781680991574. Hardcover, 192 pages. $14.99.

This is a delightful book filled with recipes, quotes, herbal lore, medicine making, and herbal pharmacy. With gorgeous, full-color pictures of the herbs and medicines, and many useful snippets, this is destined to be a well-loved classic. The book includes extensive references and a glossary that reflects the professional training of the author, but the style is light and easy to read, and the information is easily accessible for all readers. This book offers something for everyone, from the weekend herbal hobbyist who will appreciate the recipes for vitamin C tea and a soothing mixture of lavender (*Lavandula angustifolia*, Lamiaceae) and hops (*Humulus lupulus*, Cannabaceae) for eye pillows to the professional clinician who will prescribe the oregano (*Origanum vulgare*, Lamiaceae) antiviral throat spray.

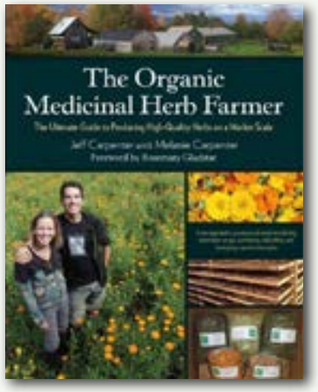
*The Good Living Guide* is organized into three parts: "Background and Getting Started," "Herbs and Their Uses," and "Preparing Herbal Remedies." These broad categories are then further divided into subsections. In Part One, for example, there are subsections for herbal medicines around the world, harvesting herbal medicines, how humans heal, and a discussion of herbs as foods and medicines. Part Two includes subsections for herbal terminology, safety, dosage, and clinical actions and applications. Part Three includes instructions for making teas, poultices, powders, medicated honeys, tinctures, vinegars, and other remedies, as well as all sorts of delicious and fragrant home and body care products.

Part Two is by far the largest section (stretching from pages 48 to 200) and contains monographs on herbs along with recipes or formulas. Each entry includes a color photo of the plant and a review of key constituents and actions, as well as recipes and formulations based on the author's clinical experience. Katolen Yardley has almost 20 years of experience as an herbal clinician, and she previously worked for more than five years as the dispensary manager at Gaia Garden Herbal Dispensary in Vancouver, British Columbia, Canada. For the past six years, she has been the herbal pharmacy instructor at the Boucher Institute of Naturopathic Medicine in New Westminster, British Columbia. Yardley uses recipes like the ones featured in this book every week and has tested them on real patients. She knows how to get an herbal cream to set, how to prevent a vinegar from turning bad, and how to use herbs to treat fungal infections.

The book has lots of useful information, and it is filled with good ideas for herbal medicine-making. However, if I could change one thing about this book, I would make it easier to navigate and find information. The herbal monographs are not listed in alphabetic order, and the table of contents does not list all of the profiled herbs or provide their page numbers. In addition, there is no master list of recipes, so I could not easily find my way back to specific ones. It was frustrating to know that there was a wealth of useful information if I could only track it down quickly. That being said, I loved the pictures and unique recipes and formulas. *The Good Living Guide* will be a valuable and well-thumbed addition to the library of all herbal enthusiasts. HG

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**Medical Herbalist, Horticulture Therapist**
**Courtenay, British Columbia, Canada**

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***The Organic Medicinal Herb Farmer: The Ultimate Guide to Producing High-Quality Herbs on a Market Scale*** by Jeff Carpenter and Melanie Carpenter. White River Junction, VT: Chelsea Green Publishing; 2015. Softcover, 416 pages. ISBN: 978-1603585736. $39.95.

*The Organic Medicinal Herb Farmer* by Melanie and Jeff Carpenter is one of the most complete step-by-step guides that I have read on what it takes to operate a functioning farm that grows and sells medicinal herbs. From the very beginning, I could almost see the dirt between the lines on the pages, which proved to me it was written by authors and other contributors with firsthand experience.

Each chapter in Part One of this book takes on topics that anyone who wants to start a farm growing medicinal botanicals needs to read and consider. Most people have a general idea of what farming is, but even farmers with experience in other crops will glean new and vital information about medicinal herb farming after reading this book. The authors guide readers through the entire process of medicinal herb farming from the decision to start growing botanicals to the sale of the final product. They discuss the proper scale to lay out a farm, which crops to grow, and all the ins and outs of postharvest handling, processing, and marketing. Each topic is well-covered and explored in enough depth for the reader to understand the choices and steps required to make their farming efforts fruitful.

From calculating the size of a manageable operation to recommending the proper plant propagation techniques, the authors throroughly answer the question posed in Chapter 1 ("Why Grow Medicinal Herbs?") and provide readers with information to make the best choices when getting started. It will help readers to better understand the parameters for making choices and how each decision will affect them later. Some of the topics covered are not glamorous, but they are essential. For example, weed control is the number-one topic and a universal problem that farmers and growers around the world face on a daily basis during growing seasons. More often than not, weed control is also one of the larger expenses that farms have, yet is too often overlooked. Whether hiring family members, day laborers, or piecemeal or contract workers, labor expenses can also become a significant part of a farm's budget.

The chapter on postharvest processing is filled with helpful information that is crucial to the success of producing and selling a medicinal herb crop, whether fresh or dried. I often see farmers grow a beautiful crop but then reduce the dollar value because of poor postharvest handling and processing techniques. The section of this chapter that was contributed by Alexander Otto is in-depth, and includes charts and graphs filled with information about the technical aspects of drying a botanical correctly to produce a high-value crop for customers.

Throughout the book, there are relevant pictures taken from the beginning of the farm to the building of the drying shed. Each picture is captioned with the details of its subject matter, which is very helpful.

Another great section of this book is Part Two, titled "Herbs to Consider Growing for Market," which contains 50 individual plant profiles. Each profile lists information about the plant species, including the life cycle, growing conditions, propagation techniques, harvest timing and other specifications, postharvest and drying, pests and diseases, anticipated yields, and pricing. To me, this detailed information is essential to getting a good start and having success with the chosen species.

I commend the Carpenters for both the creation of Zack Woods Herb Farm and the time and effort they have put into this book to help others who want to start or improve their medicinal farming operations. This will be one of the books I keep within reach on my top shelf from now on. It is a resource to which I will refer every person who calls me wanting to start a medicinal herb farm. HG

**—Edward J. Fletcher**
**Director, Quality and Sustainability**
**Herbal Ingenuity**
**Wilkesboro, North Carolina**



# Fredi Kronenberg
# 1950-2017



Respected academic researcher and American Botanical Council (ABC) Board of Trustees member Fredi Kronenberg, PhD, died at home on April 20, 2017, after a lengthy illness. Kronenberg's long and fruitful career focused on the area of women's health, particularly menopause and the study of alternative therapies for hot flashes. She championed the cause of integrative medicine in the worlds of academia and clinical research, with a particular interest in the use of plants such as black cohosh (*Actaea racemosa*, Ranunculaceae) that contain phytoestrogens. Her affiliation with ABC began in 1996, when she joined the Advisory Board as an expert source and reviewer. In 1999, she joined the ABC Board of Trustees, on which she served until her death.

After earning her bachelor's degree in neurobiology from Cornell University and doctorate in physiology from Stanford University, Kronenberg became interested in women's health and menopause during her postdoctoral studies at Columbia University. As a result, in 1989, she co-founded the North American Menopause Society (NAMS), a nonprofit organization that promotes the health and quality of life of women experiencing menopause and seeks to further understand menopause and healthy aging through a multidisciplinary approach.

Kronenberg questioned why the medical community had a general prejudice against herbal medicine, and her lifelong love of nature inspired her to pursue research on botanical-based therapies. In 1990, she attended the first Sino-American Conference on Women's Issues in China, where she observed the use of herbs for women's health issues in accordance with traditional Chinese medicine (TCM) practices. The discussions at this conference prompted her to further pursue TCM through a program at the New York Botanical Garden (NYBG), and she received a grant from the National Institutes of Health (NIH) to study and collaborate on TCM and women's health with Fudan University in Shanghai.

In 1992, Kronenberg co-founded the Richard and Hinda Rosenthal Center for Complementary and Alternative Medicine at Columbia University's College of Physicians and Surgeons, the first complementary and alternative medicine (CAM) program at an Ivy League medical center. The center, which closed in 2007, served as a blueprint for similar facilities at medical schools around the country. The Rosenthal Center attracted much support, and became an NIH-funded research center from 1994-1997 with research programs in phytochemistry, ethnobotanical studies, and clinical studies. Under the auspices of the center, Kronenberg collaborated with ABC Advisory Board member Edward Kennelly, PhD, to research the constituents and effects of black cohosh.

The Rosenthal Center had a strong educational mission, and it sponsored a continuing medical education course in botanical medicine for health care practitioners interested in integrating alternative medicines and therapies into their practices. The course, "Botanical Medicine in Modern Clinical Practice," held at Columbia University and the NYBG, ran for 10 years and was co-directed by Kronenberg, Michael Balick, PhD, and Andrew Weil, MD.

Christine Wade, MPH, worked closely with Kronenberg at the Rosenthal Center. "Fredi was dedicated to women's health care choices as a very young scientist," Wade wrote (email, May 2, 2017). "She was the first physiologist to describe a common thermoregulatory process (hot flashes at menopause) in women. Her subjects were a subset of women who were afflicted by many or long periods of hot flashes.... Discussions with the women she studied led to a long career of investigating how women navigate their health and increasing evidence-based treatment options for conditions that women suffer and that health care systems often ignore. She courageously and resiliently never let go of the importance of such questions."

Kronenberg was a founding editor of the *Journal of Alternative and Complementary Medicine* and served on the editorial board for numerous publications, including *Menopause*, *Journal of Tropical Medicinal Plants*, *EXPLORE: The Journal of Science and Healing*, and *Journal of Women's Health*. She was also a founding member of the Consortium of Academic Medical Centers for Complementary and Alternative Medicine. In addition to the many research articles she authored and co-authored, Kronenberg collaborated with Raymond Cooper, PhD, on the book *Botanical Medicine: From Bench to Bedside* (Mary Ann Liebert Inc., 2009).

At the time of her death, Kronenberg was affiliated with the Arizona Center for Integrative Medicine, the University of Arizona College of Medicine, and the NYBG, in addition to ABC. She also held a position at Stanford University's Clayman Institute for Gender Research, where she conducted research on hot flashes and worked with colleagues to expand Stanford's integrative medicine program.





As a visiting scientist at the NYBG, she worked closely with Balick, who is also an ABC Board of Trustees member, on a collaborative ethnomedicinal project in New York City that examined medicinal plants used by different ethnic communities in the city. This work helped develop a field of study known as urban ethnobotany.



Fredi Kronenberg and Mike Balick
Photo ©2017 Steven Foster

**"Fredi [brought] dignity, humility, inquisitiveness, humor, empathy and an extraordinary sense of kindness and camaraderie to whatever she [was] involved with. She [did] so much for so many people, shaping the trajectory of their lives and career paths in a very positive and innovative way, while at the same time asking for nothing in return — a true scholar, idealist, visionary, friend, and champion of integrative medicine."**

In Kronenberg's 2010 profile in issue 85 of *HerbalGram*, Balick was quoted as saying: "Fredi brings dignity, humility, inquisitiveness, humor, empathy and an extraordinary sense of kindness and camaraderie to whatever she is involved with. She has done so much for so many people, shaping the trajectory of their lives and career paths in a very positive and innovative way, while at the same time asking for nothing in return — a true scholar, idealist, visionary, friend, and champion of integrative medicine."[1]

"This [quote] is as true today as when I wrote it back in 2010," Balick commented (email, May 4, 2017), "and a fitting tribute to my dear friend."

Kronenberg's work for the mission of ABC cannot be understated, said ABC Founder and Executive Director Mark Blumenthal. He added:

> ABC owes so much to Fredi, and her contributions are difficult to measure. She was connected to many people in the alternative and complementary medicine world and directly and indirectly introduced them to me, particularly through her invitation to participate on the faculty of all 10 of her week-long botanical medicine training courses at Columbia. In addition to Fredi's direct role on the ABC Board of Trustees, she is responsible for many of the professional affiliations and personal friendships that have had an indelible impact on the direction of ABC's research and educational programs over the years.



Fredi Kronenberg and
Mark Blumenthal
Photo ©2017 Steven Foster

John Cardellina, PhD, former vice president of botanical science and regulatory affairs at the Council for Responsible Nutrition (CRN), also recalled Kronenberg's friendliness and acumen. "She was among the first key players in the botanical world that I met when I came to CRN," he wrote (email to M. Blumenthal, April 22, 2017). "She was welcoming and helpful to me, and always took a minute to say 'hi' and catch up. She will always stand out in my mind as one of the really good people and knowledgeable scientists in this field."

Kronenberg received numerous recognitions and accolades for her work in women's health and in the field of herbal medicine. She was named as one of "Ten Heroes for Women's Health" in 1997 after receiving the American Health for Women Award, and was recognized by NAMS with its A Friend Indeed Award. Kronenberg also received the 2004 NAMS/GlaxoSmithKline Consumer Healthcare Botanicals Research Award, the 2005 NAMS/Duramed Pharmaceuticals Vasomotor Symptoms Research Award, the 2008 NAMS/Amerifit Brands Complementary and Alternative Medicine Research Award, and, most recently, a clinical research prize from the European Society of Integrative Medicine for a study that she co-authored.[2]

In her spare time, Kronenberg was an avid photographer, and colleagues often remember her with a camera in hand, taking thousands of pictures during travel and field trips. She also enjoyed music, particularly folk, jazz, classical, and bluegrass. "I grew up with folk music, as my mom played guitar, and as soon as I was big enough to pick one up, I learned to play," Kronenberg was quoted as saying in her *HerbalGram* profile.[1]

Jacqueline Wootton, founder and former editor

of the HerbMedPro database, acknowledged Kronenberg's wide array of accomplishments and her commitment and passion for her work. "Fredi was always kind, generous, and positive," she wrote (email to M. Blumenthal, April 28, 2017). "Her warm smile and support encouraged her team to excel in their goals. Fredi was ever open to innovative suggestions and eager to explore new ideas and assess their potential. Her questions and challenges were perceptive and insightful, leading to finely honed, enduring projects. Never a self-publicist, Fredi quietly made a large impact on the field of botanical and integrative medicine."

Other colleagues similarly remember Kronenberg's years of dedication. "I learned from and worked with Fredi for the past 16 years on the New York Botanical Conference, a joint initiative between Columbia University and the University of Arizona, and on the Nutrition and Health Conference," wrote Victoria Maizes, MD, executive director of the Arizona Center for Integrative Medicine and a professor of medicine, family medicine, and public health at the University of Arizona, in a listserve dated April 25, 2017. "She was … a passionate pioneer with many innovative ideas! She was easy to love and admire. She lived life fully."

Tieraona Low Dog, MD, praised Kronenberg's commitment to CAM research and education. "Integrative medicine lost a leader in the research community," she wrote (email, May 4, 2017). "Whether studying bees during grad school or black cohosh in women transitioning through menopause, Fredi had a deep curiosity of the world. Her open-mindedness towards herbal and complementary medicines was only dwarfed by her big open heart, a warm place that she allowed so many of us to dwell. She will be deeply missed."

Fredi Kronenberg is survived by her mother Honey, sister Kim, brother-in-law Allen, and stepfather Gene. She was 67 years old. HG

**—Hannah Bauman**

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## James A. May, Sr.
## 1936-2017



James May, hailed as the "father of stevia," died after heart complications on February 28, 2017. May left a long and successful career as a health care executive and an internationally known specialist of end-stage renal disease after a friend introduced him to the sweet plant stevia (*Stevia rebaudiana*, Asteraceae). Recognizing the potential for an alternative, natural sweetener in the US market, May founded Gilbert, Arizona-based Wisdom Natural Brands in 1985 and began the long legal journey to convince the US Food and Drug Administration (FDA) of stevia's safety as a food.

Native to Paraguay and Brazil, stevia had been used by the Guaraní people of the region for more than 1,500 years as a sweetener. The plant became popular in Japan as it replaced synthetic sweeteners in food products and sodas in the 1970s. However, when May began importing the plant to the United States, it was relatively unknown outside of natural food retail channels. After the passage of the Dietary Supplement Health and Education Act of 1994, the FDA revised its 1991 full import ban of stevia and recognized the plant and its extracts as dietary ingredients, but May's battle continued: Wisdom Natural Brands received a warning letter in 2004 from the FDA due to the presence of whole-leaf stevia in its products, which the FDA considered "an unsafe food additive."[1] (Unlike foods and dietary ingredients, food additives require FDA pre-market approval that involves the FDA's review of relevant literature to determine the proposed additive's safety.)

Under May's leadership, Wisdom Natural Brands pioneered the formulation of stevia-based sweeteners through its development of a water-membrane filtration and extraction system. The company's SweetLeaf extract was the first to gain Generally Recognized as Safe (GRAS) status in March 2008, followed shortly thereafter by products from industrial giants such as Cargill in collaboration with the Coca-Cola Co. later that year. However, the GRAS designation only applies to "highly purified" rebaudioside A, one of the primary components responsible for stevia's sweet taste, and does not apply to whole-leaf stevia or crude stevia extracts.[2]

In his business pursuits, May worked closely with the farmers and growers of his stevia in the plant's native Paraguay. He contributed to research for the ideal growing methods to enhance the plant's flavor, increase yields, and produce a better crop for the market. May's efforts earned him personal recognition from Frederico Franco, the president of Paraguay, in 2012. Today, the stevia market is worth almost a billion dollars annually.

May received the American Herbal Products Association's (AHPA's) very first Visionary Award in 2011, an award created in his honor. Further industry recognition came from the Specialty Food Association, which awarded May the 2015 Visionary Leadership Award, and from New Hope Natural Media at its Natural Products Expo West, which inducted May and his wife Carol into its Hall of Legends in 2016.

AHPA President Michael McGuffin expressed his appreciation for May's work in the natural products industry and mourned his passing, writing, "Throughout his life, Jim demonstrated unwavering, persistent dedication to advancing all-natural stevia, working for more than 25 years to achieve regulatory approval. He has been widely lauded for his leadership in spawning a new industry."[3]

"Jim May was one of those rare people who has helped to define the natural foods and herb industries," said American Botanical Council (ABC) Founder and Executive Director Mark Blumenthal. "Jim was a highly-committed 'true believer,' a person who was devoted to the value proposition that there was a rightful place in the market for a safe, natural, relatively low-cost, non-caloric plant that could be used as a food and as a sweetener. Despite considerable opposition from a then-obstructive FDA, Jim kept his focus and his attention on pushing for acceptance of stevia. Millions of Americans, and other consumers around the world, owe him a deep debt of gratitude, as do we at ABC for his long-time support of ABC's nonprofit educational mission."

May's friends and colleagues remember him as a business leader, a stalwart member of his community, and a dedicated husband and father. He is survived by his wife Carol; children Stephen, Michael, Shannon, and Erin; seven grandchildren; and his sister Ramona Sterling. He was preceded in death by his children James and David. Wisdom Natural Brands states that it will continue as a family business, with Carol May as president and Michael May as chief operating officer. HG

**—Hannah Bauman**

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# Bernard Ortiz de Montellano 1938-2016



Aztec traditional medicine expert Bernard Ortiz de Montellano, PhD, died on December 2, 2016, in Austin, Texas, after a short battle with liver cancer. Ortiz de Montellano combined a lifelong interest in Mesoamerican culture with rigorous education in chemistry and anthropology to impart knowledge of Aztec society and accomplishments to his students.

Born in Mexico City on August 31, 1938, Ortiz de Montellano came to the United States from Mexico to pursue his college education at the University of Texas – Austin, and earned his doctoral degree in organic chemistry in 1965. His research focused on the health and nutrition practices of the Aztec people of central Mexico. He taught at St. Mary's University in San Antonio, Texas, and the University of Utah in Salt Lake City before he transferred to Wayne State University in Detroit, Michigan, in 1976. He taught at Wayne State until his retirement in 1998. After retiring to Austin, Ortiz de Montellano continued to mentor, teach, and lecture.

Michael Heinrich, PhD, a pharmacognosist at University College London, was mentored by Ortiz de Montellano in the early years of his career, and remembered him as "keen to debunk pseudoscience and unsubstantiated scientific claims" about the history of pre-colonial American societies (email to M. Blumenthal, February 2, 2017). "He was an enthusiastic scholar of all aspects of Mexican and, most importantly, Aztec life, who brought together a tremendous expertise in chemistry and Mesoamerican studies," Heinrich wrote. "I want to remember his keen interest in ascertaining that all research is evidence-based and founded in a careful factual assessment of the primary data."

Ortiz de Montellano published more than 40 articles and several books, including *Aztec Medicine, Health, and Nutrition* (Rutgers University Press, 1990). His paper "Empirical Aztec Medicine," published in 1975, was an assessment of the effectiveness of Aztec medicinal plants.[1] Ortiz de Montellano drew from 16th-century codices compiled by Spanish missionaries, and separated the more widely studied relationship between spirituality and health from the use of medicinal plants prescribed by Aztec physicians. Botanicals listed in the codices included avocado (*Persea americana*, Lauraceae), cacao (*Theobroma cacao*, Malvaceae), and papaya (*Carica papaya*, Caricaceae), all of which, he concluded, would have produced effective results according to their recorded uses in the codices. The codices translated by Ortiz de Montellano described a society with a strong practice of herbal medicine and use of plants for health and wellness.

He also studied the grislier aspects of Aztec culture. His paper "Counting Skulls" countered the prevailing theory of Aztec cannibalism as ecological necessity.[2] "While it is well known that such practices exist," wrote Heinrich, "they must be understood in the cultural context." Ortiz de Montellano proceeded to re-create that historical context through the examination of archaeological evidence and his own independent research. Perhaps inevitably, this morbid line of questioning, such as his calculations of the total amount of human flesh obtained through sacrifice and the relative share of protein in a human body, raised a few eyebrows. "It did take a long time," Heinrich recalled, "to convince the [Detroit] coroner." However, Ortiz de Montellano eventually concluded that "the Aztec diet was adequate in protein and cannibalism would not have contributed greatly."[2]

Eloy Rodriguez, PhD, professor and research scientist at Cornell University, called Ortiz de Montellano a "great friend, mentor, and scholar, dedicated to social justice" (email, April 11, 2017). "His two major publications on the Aztecs and phytomedicine provided brilliant insights into culture, plant chemotaxonomy, organic chemistry, disease treatments, and pharmacology. Bernard was also a superb teacher, fluent in Nahuatl, language of the Aztecs or Mexicas, and in Spanish."

Ortiz de Montellano's great passion in life came from educating the next generation of young learners. Eager for young Chicano and Native American students to succeed in science and technology, he helped co-found the Society for Advancement of Chicanos/Hispanics and Native Americans in Science (SACNAS). Through SACNAS, he taught workshops to K-12 students and served as a mentor. He was also a fierce advocate for civil rights, particularly prison reform in Texas. He remained politically active throughout his career and well into his retirement, volunteering at the Volunteer Health Clinic in Austin and teaching continuing education courses on anthropology and the cultures of ancient Mexico at the University of Texas.

"Bernard was a great transdisciplinary scientist, whose ideas were well ahead of what people thought and researched at the time," wrote Heinrich. "He was a proud Chicano — both Mexican and US-American." Ortiz de Montellano is survived by his wife Ana Mercedes; his two sons Bernardo and Victor; four grandchildren; and his brother Paul. He was preceded in death by his parents Bernardo and Thelma and his sister Ana Luisa. A memorial celebrating his life was held in Austin in January 2017. HG

**—Hannah Bauman**

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# Elwood Richard 1931-2017

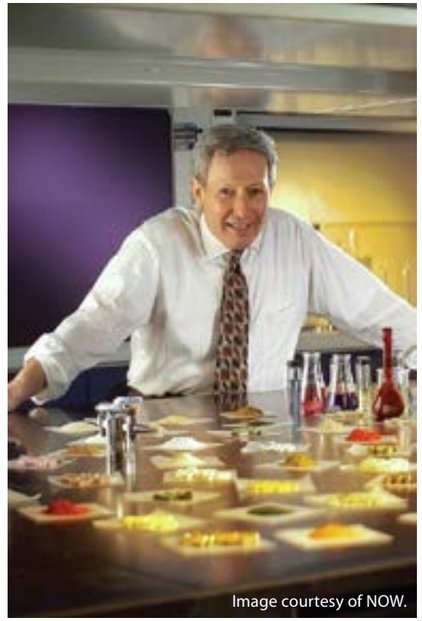


Image courtesy of NOW.

Elwood Richard, founder of natural products and dietary supplement industry leader NOW, died on April 7, 2017, after a lengthy battle with mesothelioma. He will be remembered for the significant impact he made on the natural food and dietary supplement industries over the course of almost six decades.

Richard's introduction to natural foods began when his father, Paul Richard, bought Fearn Soya and developed the industry's first soy (*Glycine max*, Fabaceae) protein supplement product. Elwood Richard, with a bachelor's degree in chemistry from Monmouth College in Monmouth, Illinois, and graduate studies in physical chemistry and biochemistry at Indiana University, stepped in to run Fearn in 1960 after his father's death, with input from his brothers Bill and Lou. In 1962, Richard opened his first health food store, the Health House. Eventually renamed The Fruitful Yield, the Chicago-based retail chain currently operates 13 stores. In 1968, Richard founded NOW. His brother Lou would later join the company full time, and together they worked with early quality programs of the National Nutritional Foods Association (NNFA, now the Natural Products Association [NPA]) Standards Committee.

Richard led NOW through decades of growth, expanding product lines and manufacturing facilities, and he never wavered from his original belief that good health should be available to everyone. He also ensured that the company's mission of empowering people to lead healthier lives would never be compromised by short-term profit demands. Through Richard's legacy planning and gifting of shares to family members, NOW currently has about 40 owners from the Richard family, and it is well positioned for future generations, according to information on the company's website.

When Richard retired as CEO in 2005, succeeded by longtime Fruitful Yield and NOW employee Al Powers, he stayed very much involved in the business and the industry as the chair of the NOW Board of Directors, and a member of the NOW Advocacy Team, the NOW Strategy Team, and the NOW Environmental Team. He was also on the managing board of the Natural Health Research Institute (NHRI), a nonprofit organization he founded that is committed to informing consumers, scientists, the media, policymakers, and legislators about scientific evidence on the usefulness and cost-effectiveness of a good diet, supplements, and a healthy lifestyle.

NOW CEO Jim Emme, a veteran of the company for 22 years, commented: "His passion in defending consumer choice in the industry with logic and with scientific knowledge he had as a physical chemist came through many, many times. One of the legacies he left is the Golden Rule, treating others as you want to be treated. He lived that every day that I knew him."

Former NOW CEO Powers also recalled Richard's energetic commitment to the company's mission. "El was a truly great man and a great entrepreneur. He was always passionate about the health food industry, and the success of the NOW brand is a testimony to his vision, leadership, and dedication to our mission and our industry. He will always be remembered for his love, generosity, and kindness that touched the lives of everyone at NOW. He was the heart and soul of NOW Foods."

"This year is my 20th year working for Elwood Richard's companies," wrote Neil E. Levin, CCN, DANLA, a nutritionist, writer, and educator who works at NOW (email to M. Blumenthal, April 14, 2017). "I found him to be unfailingly polite, kind, inquisitive, generous, and fully committed to the natural products industry. He was always interested in me, both as an employee and as a fellow natural products enthusiast, frequently taking time to ask about me, my work, and my family, including my wife's organic garden."

"His work ethic, deep faith, tolerance, family values, and belief in the Golden Rule have driven the success of his businesses without losing the love and respect of his family, friends, employees, customers, and even business competitors," Levin continued. "He constantly visited health food stores when traveling, even when on vacation. He freely shared best practices and quality methods developed by his employees with the industry without trying to patent or restrict their use for profit, because he believed that we all sink or swim together. He was especially concerned about health freedom and product quality issues, devoting much of his energy to these areas. This focus culminated in his work to support the NHRI, a long-term project close to his heart."

Richard was recognized by the industry he served for so many decades with numerous honors and awards, including induction into the New Hope Hall of Legends, the NPA Lifetime Achievement Award, the *Nutrition Business Journal*

Lifetime Achievement Award, the NNFA Crusader Award, and, most recently, the American Herbal Products Association (AHPA) Visionary Award.

After the announcement of Richard's death, his fellow industry leaders came forward to honor his life and legacy. United Natural Products Alliance President Loren Israelsen commemorated Richard's life in a public comment, stating: "We note with sadness the passing of one of the industry's true legends, who, as much as anyone in living memory, has shaped the modern natural foods and dietary supplement industries. Elwood combined extraordinary tenacity with a very clear focus on and vision for what he was hoping to accomplish: combining value and quality in his company's products and to continually invest in his business. He was a force of nature…. His legacy lives on through the NOW team and its continued support of best practices and multiple industry quality initiatives" (email, April 11, 2017).

AHPA President Michael McGuffin was quoted as saying, "I was honored to acknowledge Elwood with the AHPA Visionary Award earlier this year, adding to the already impressive list of awards and honors bestowed upon him by the natural products industry…. His sincere and lifelong commitment to public health greatly benefitted the industry and the public. He will be sorely missed, but his rich legacy makes Elwood impossible to forget."[1]

Dan Fabricant, PhD, executive director and CEO of the NPA, remembered Richard's business savvy and personal involvement with NOW. "One of the things that was so remarkable was that he hired good people and got out of the way," said Fabricant in a statement to NutraIngredients-USA.[1] "He looked to others to add strength, and so many business owners could learn from that."

In the same article, Steve Mister, president and CEO of the Council for Responsible Nutrition, was quoted as saying, "[Richard] was a true pioneer in the dietary supplement industry and a strong advocate for supplement consumers…. [H]is passion for 'empowering people to lead healthier lives' came across in every conversation, every communication, and to everyone who had the opportunity to know and work with him."

American Botanical Council Founder and Executive Director Mark Blumenthal added: "El was always a consummate gentleman and a true believer in the proposition that natural foods and dietary supplements are necessary elements of a healthy life. He is a genuine pioneer of the natural products community and a strong example of the uniqueness and special character of the people in this community."

Elwood Richard is survived by his wife Betty, daughter Sharon (Richard) Wong, sons Dan and David, five grandchildren, and one great grandchild. "His sincere humility and great humanity live on in the hearts of his family and friends, and in the ethical and responsible business practices of his company," concluded Levin. "He will be missed, but will always remain with those who knew him." HG

**—Hannah Bauman**

***Editor's note:*** *We would like to thank NOW Health Group, Inc., and Neil Levin for their contributions to this tribute, including the use of language from a press release[2] and tremendous insight from Mr. Levin.*

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***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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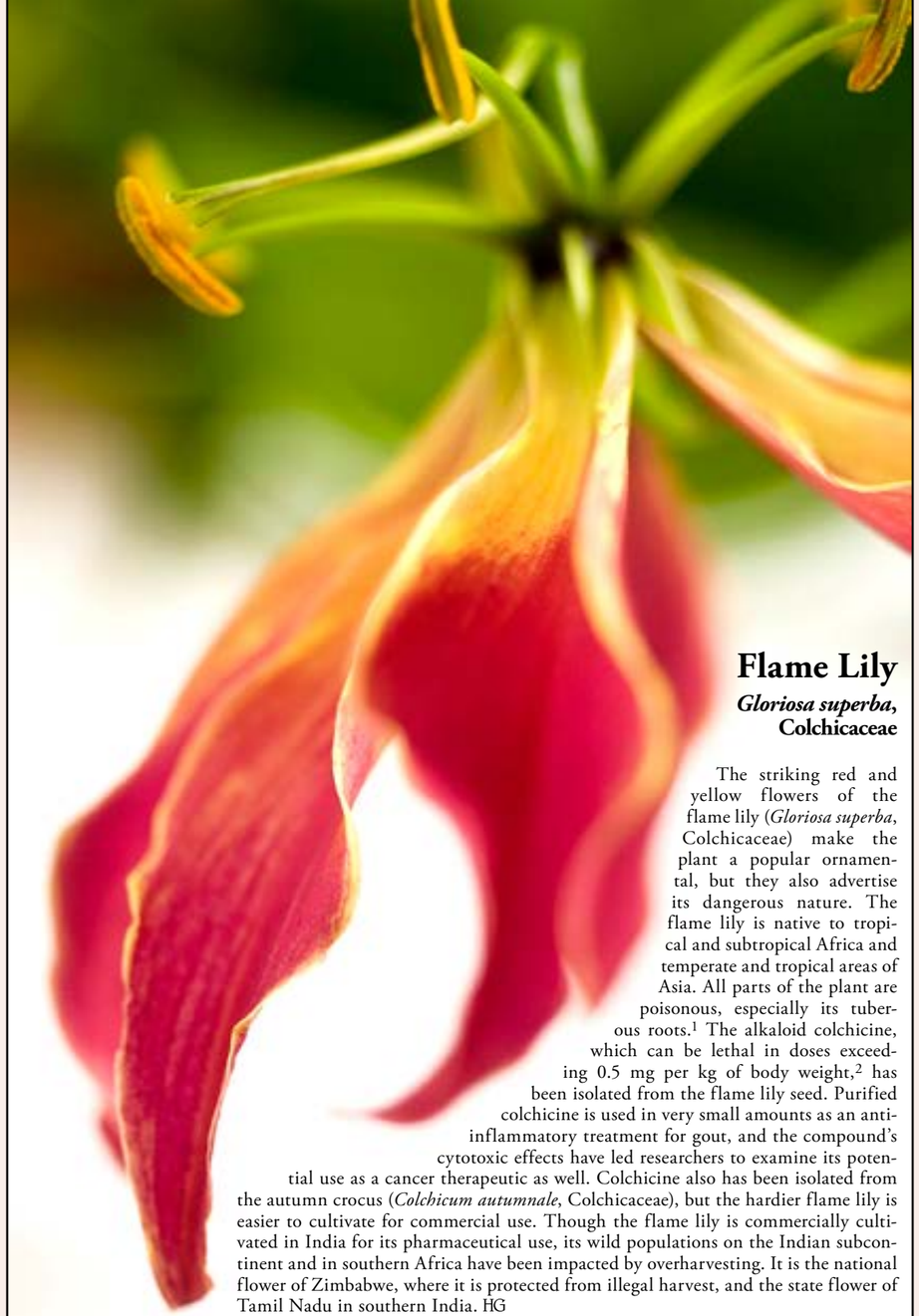
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## Flame Lily

***Gloriosa superba*, Colchicaceae**

The striking red and yellow flowers of the flame lily (*Gloriosa superba*, Colchicaceae) make the plant a popular ornamental, but they also advertise its dangerous nature. The flame lily is native to tropical and subtropical Africa and temperate and tropical areas of Asia. All parts of the plant are poisonous, especially its tuberous roots.[1] The alkaloid colchicine, which can be lethal in doses exceeding 0.5 mg per kg of body weight,[2] has been isolated from the flame lily seed. Purified colchicine is used in very small amounts as an anti-inflammatory treatment for gout, and the compound's cytotoxic effects have led researchers to examine its potential use as a cancer therapeutic as well. Colchicine also has been isolated from the autumn crocus (*Colchicum autumnale*, Colchicaceae), but the hardier flame lily is easier to cultivate for commercial use. Though the flame lily is commercially cultivated in India for its pharmaceutical use, its wild populations on the Indian subcontinent and in southern Africa have been impacted by overharvesting. It is the national flower of Zimbabwe, where it is protected from illegal harvest, and the state flower of Tamil Nadu in southern India. HG

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2. Finkelstein Y, Aks SE, Hutson JR, et al. Colchicine poisoning: the dark side of an ancient drug. *Clinical Toxicology*. 2010;48(5):407-414. Available at: www.tandfonline.com/doi/abs/10.3109/15563650.2010.495348?journalCode=ictx20. Accessed April 20, 2017.


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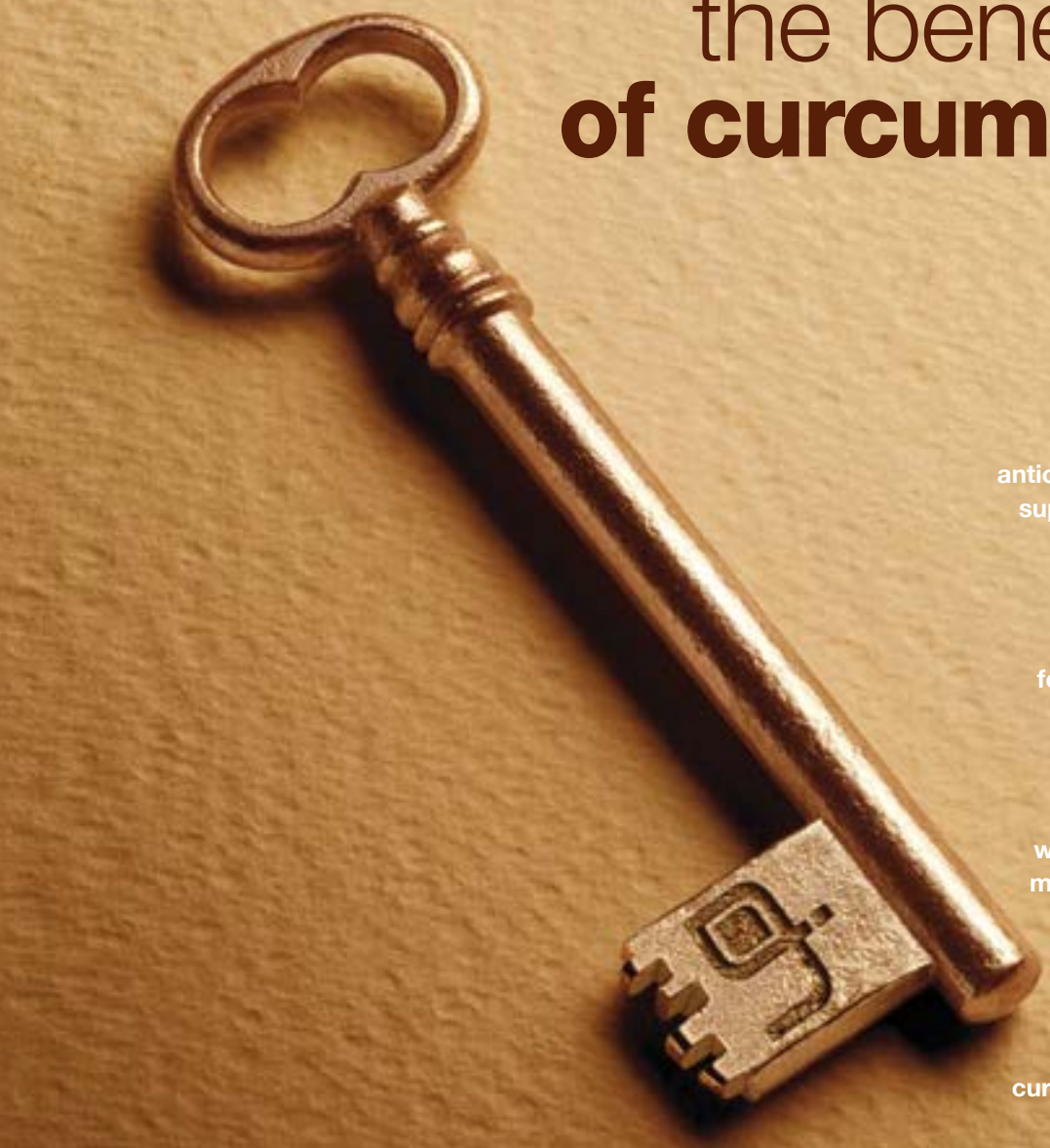
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